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CONTENTS

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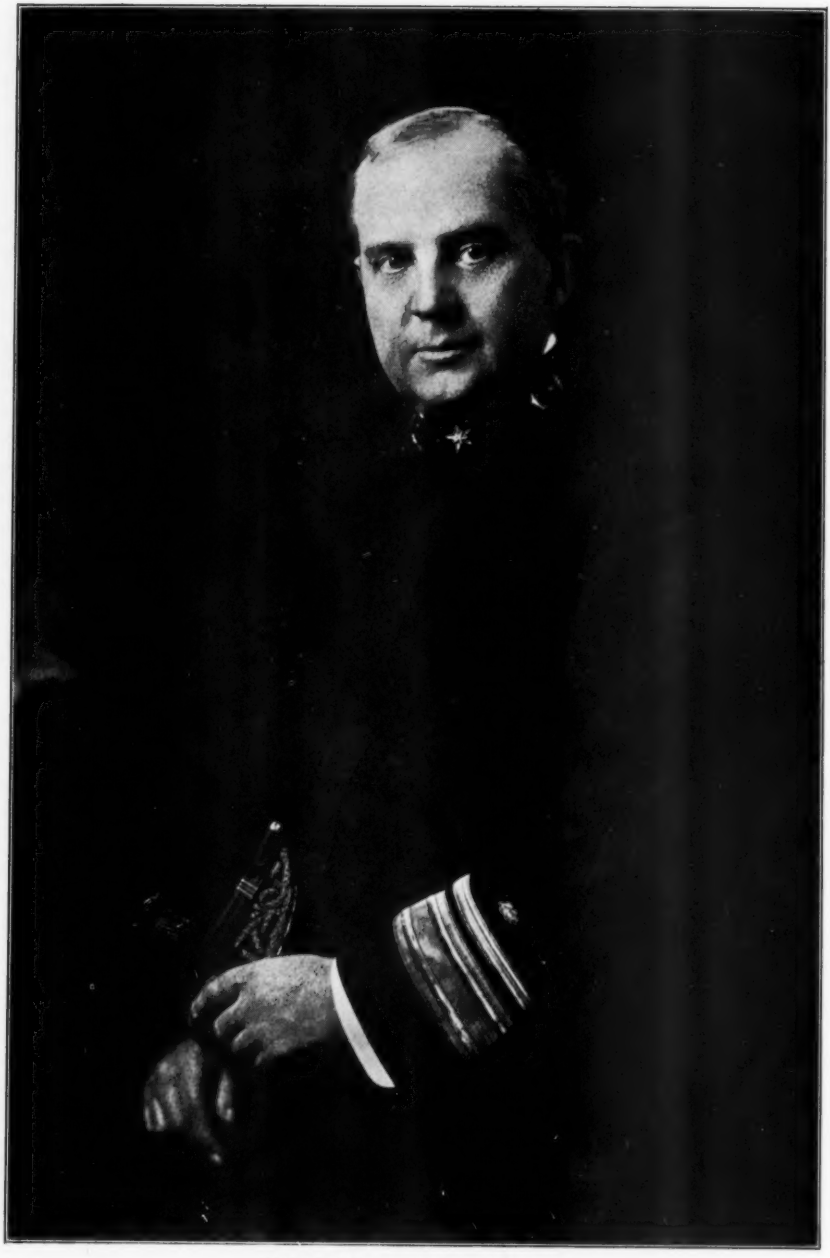


WILLIAM C. BRAISTED, M. D.

President of the Philadelphia College of Pharmacy.

THE AMERICAN
JOURNAL OF PHARMACY

Vol. 93 June, 1921 No. 6

YESTERDAY.

TODAY.

A MESSAGE FROM THE NEW PRESIDENT OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

In assuming the duties of President of the College of Pharmacy and Science of Philadelphia, I do so with a full realization of the responsibility involved; also that it is a transitional period in the affairs of the institution, which makes it a peculiary critical and important period if the College is to maintain and carry on the splendid record of the years gone by. No one person can make success, but I am counting on the undivided and loyal co-operation of every member of the College and I shall do everything I can at once to put the institution in shape for active, progressive effort.

William O. Braisted.

TOMORROW.

WILLIAM C. BRAISTED, M. D.

President of the Philadelphia College of Pharmacy and Science.

To lead the College into the second century of growth and service the members have chosen as its President, Rear Admiral William Clarence Braisted, former Surgeon General of the United States Navy, President of the American Medical Association, and Chairman of the National Board of Medical Examiners.

Throughout the World War and the period of demobilization Admiral Braisted had command of the Navy's Bureau of Medicine and Surgery, and his conspicuous services gained for him an international reputation for broad vision and efficient administration. Secretary Daniels' Report of the Navy's activities in the War is in reality a tribute to the services of Admiral Braisted. That report says:

"Recognition of the excellence of the work of the Medical Department of the Navy, under the direction of Surgeon General Braisted, has come from medical authorities at home and abroad. At the last session of the American Medical Association Admiral Braisted was elected its President, the highest honor that can come to an American physician. This was not only a tribute to the Surgeon General, but a tribute as well to the Naval medical force. It is gratifying also to know that he has been made an Honorary Fellow of the Royal College of Surgeons of Edinburgh, one of the few Americans upon whom this honor has been conferred."

Admiral Braisted was born in Toledo, Ohio, on October 9, 1864. In 1883 he was graduated a Bachelor of Philosophy from the University of Michigan. Three years later, when he was graduated a Doctor of Medicine from Columbia University, he was an honor man in his class. After two and a half years of service in Bellevue Hospital in New York he practiced medicine in Detroit until, in September, 1890, he entered the Navy as Assistant Surgeon.

Step by step William C. Braisted advanced in the service, serving on many vessels and at many naval hospitals. Twice he was instructor in surgery in the Naval Medical School. For zeal and skill in caring for the wounded after the battle of Puerto Cabello he was decorated with the Order of Bolivar by the President of Venezuela. In 1904, he fitted out and equipped the hospital ship "Relief."

During the Russo-Japanese War he represented the Medical De-

partment in Japan and was decorated by the Mikado. As Assistant Chief of the Bureau he assisted in the complete reorganization of the medical service of the Navy. For a time he served as Attending Physician at the White House in the administration of President Roosevelt.

From 1912 to 1914, he was Fleet Surgeon of the Atlantic Fleet. In 1913, he was elected President of the Association of Military Surgeons of the United States. February 18, 1914 he was appointed to the post of Surgeon General and Chief of the Bureau of Medicine and Surgery, with the rank of Rear Admiral.

Upon the shoulders of Admiral Braisted fell the responsibility for the surgical, medical and pharmaceutical readiness of the Navy in the World War, not only in the matter of supplies, but in personnel also. So well did he perform his task that every call made upon the bureau was answered. To his care nearly 120,000 sick and wounded soldiers, sailors and marines were entrusted; his jurisdiction extended over the Marine units fighting in France, over the Naval aviation stations, over health conditions in submarines and the Sanitary and Medical features of the transportation of the Army to Europe accomplished by the Navy in fact, over the myriad activities touched upon by the Naval forces.

An idea of the magnitude of his task may be obtained from the fact that of 1,235,933 American troops returned by June 20, 1919, 111,522 of them were sick or wounded and in his keeping.

Admiral Braisted has brought about the reorganization and enlargement of the Medical and Hospital Corps by securing necessary legislation for increased personnel with increased rank and pay. He has secured hospital construction and administration of the most up-to-date kind of the Navy. He has founded four colleges at Newport, Norfolk, the Great Lakes Training Station and San Francisco, respectively, for the training of Naval pharmacists. In addition he established a correspondence course in pharmacy for men in the Navy's Hospital Corps. The first hospital ship of the Navy to be designed and fitted out from the keel up for the special purposes of the Medical Department, now under way at the Navy Yard at Philadelphia, was undertaken under his auspices. He has had prepared the book of instructions for the Hospital Corps, as well as the Manual of the Medical Department for Medical Officers, the Compend for Masters of Auxiliary Vessels, special reports on the War in Europe, etc.

Recognition of the distinguished services of Admiral Braisted has not been lacking. Among the honors accorded him are the degree of Doctor of Laws by the University of Michigan and Jefferson Medical College, and the degree of Doctor of Science by Northwestern University. He is President of the Board of Visitors of the Government Hospital for the Insane, a member of the Board of Regents of the American College of Surgeons, a Director of Columbia Hospital in Washington, and once Vice-Chairman of the War Relief Board of the American Red Cross. During the war he was a member of the Central and Executive Committee of that body.

He is President of the National Board of Medical Examiners and a member of the American Medical Association, the Southern Medical Association, the American Academy of Medicine, and many other societies. Dr. Braisted is also Chairman of the Provisional Board of the Gorgas Memorial Institute begun recently at Panama, a great institution for research into tropical diseases and preventive medicine for the welfare of the entire world.

For his services during the war he was awarded the Distinguished Service Medal of the Navy.

EDITORIAL

LOOKING FORWARD.

It is not the mystic number one hundred, or the recent centennial celebration, but the necessity for adjustment to present-day conditions, that has brought about the expansion of the Philadelphia College of Pharmacy and Science. The marvelous progress of science—the advent of labor-saving machinery, to which is due the development of large pharmaceutical manufacturing establishments—the advances in medicine, particularly in diagnosis, calling for trained bacteriologists and clinical chemists—all these have trended toward specialization by students in pharmacy, and opened new fields of service for the institution.

To be sure, the founders established a college of apothecaries. But the old-time apothecary is no more. He has gone the way of the tallow candle, and the Franklin stove. His place has been taken by the modern prescriptionist, and the manufacturer of medicinal

products, the assayist and control chemist, the bacteriologist, the clinical chemist and hospital technician, the distributor of sick-room appliances, the manager of the modern drug emporium, and the merchant prince dealing in drugs on an extensive scale.

So there have been added from time to time courses of training for these specialists; and the founders would be astonished as much by the present-day diversity of functions of their College, as they would be by the present-day appearance of their beloved Philadelphia, with its tall buildings, its trolley cars, automobiles, telephones, and electric light.

There comes now the necessity not only for more specialization, but for courses in the basic sciences, so that our students may have the advantages of a broader and stronger foundation upon which to rear the superstructure of special training. This will bring to them greater possibilities in pharmaceutical research, for it will provide new methods of attack in the solving of research problems.

To supply these basic courses, the College must have added facilities, which can be provided only in new and larger buildings, specially planned to meet our needs. Such buildings call for an appropriate setting, and a proper environment. Hence the plan of new buildings on the Parkway, or in the suburban districts.

But buildings fill only material needs; and there are in prospect accessions to the faculty—men who will administer the courses in the languages, in mathematics, in physics, and in physical chemistry, and make possible plans of study which conform to the best academic standards, and at the same time provide training for a specific line of activity in some pursuit associated with the sciences of medicine, or with health problems.

To direct the work in an institution such as this College has come to be, and to fully develop its potentialities, there is needed a man conversant with academic traditions, trained in science, experienced as an executive, and capable of bridging the chasm which the years have worn and which now unhappily separates the medical investigators from the group of research workers dealing with the pharmaceutical and chemical aspects of medicinal products.

And Admiral William Clarence Braisted, President of the American Medical Association, who is pre-eminently qualified to render this exceptional service to the College and to pharmacy and medicine, has accepted the call of the presidency to carry to a splendid consummation the extensive educational program projected, and

the material development which it necessitates. His charming personality and his renown will be an inspiration. His past achievements guarantee success. Alumni, faculty and college officers stand ready to give him their enthusiastic support.

—The Site on the Parkway:—it will be secured. The New Buildings:—the plans are under way. The Money for this pretentious development in all its branches:—it will be forthcoming when needed. The Leader who can guide us to wider fields of service:—he has been found.

The vision of a greater Philadelphia College of Pharmacy and Science, a fitting memorial to the founders and to all who participated in the upbuilding of the College in the years past, will soon become an actuality. J. W. S.

EXAMINATION AS A MEASURE OF ABILITY.

No experienced teacher ever expects an examination or even a series of examinations, to yield mathematically accurate results in measuring the ability of a student. The values obtained are only relative and must be considered in connection with other factors in passing final judgment upon any applicant who is subjected to such a test.

An examination is sometimes a measure of capacity or of retentiveness or of concentration, if it follows close after the presentation of a subject, but it can never be considered as an infallible index of mental qualifications.

If this be true of specific examinations covering a single subject or a limited range, how much less value can be placed upon examinations which are known as "general information tests." And yet there is an element of value here which must not be overlooked.

Much comment has resulted the making public of a list of questions which it is said, has been used by Thomas A. Edison in passing upon applicants for positions in his employ. Many prominent educators and professional men have seen fit to criticize Mr. Edison and deride his plan as of no value for the purpose.

How do these individuals know Mr. Edison's purpose? He has not revealed it. His published comment which brought the storm about him was to effect that "college graduates are amazingly ignor-

ant." Perhaps this is so, and perhaps this fact is made plain by just such a test as Mr. Edison applied if rightly interpreted. The kind of questions used by Mr. Edison are apparently of the general information type. This type of questionnaire is found as one of the subdivisions of the Alpha Army Intelligence Test, to which a million or more American youths were subjected while in the training camps during the war.

Information for its own sake is of little value. It is ordinarily regarded as haphazard or casual as opposed to knowledge which is accurate and systematic. Learning is superior to information and is the result of study. Wisdom is said to be applied knowledge. Information therefore may be looked upon as an amorphous form of knowledge and as such is one of the fundamental factors of wisdom.

Exposure to sources of information does not always result in the infection of the individual, else proofreaders would be among the wisest in the land or the best informed, which they usually are not.

If one studies Mr. Edison's questionnaire, however, one is impressed by the fact that it can be resolved into a number of groups of allied or associated questions concerned with such subjects as physics, chemistry, geography, history and literature to mention the most outstanding.

Is it not possible, therefore, that Mr. Edison by picking out the answers to certain questions and groups of questions may be able to classify his applicants according to their predilections and hobbies? And is it not also possible that, when one finds a large number of applicants whose knowledge is so vague and incomplete that no single subject is even passably covered, a conclusion could be drawn similar to that expressed by Mr. Edison?

All of the critics of Mr. Edison's questionnaire have assumed that he was trying to find men who were capable of making a perfect mark. This is to be doubted. What he was probably trying to do was to find men who knew all about some one subject, and in addition had a fairly wide range of general information. A man who could answer all of the questions would probably be shunned by Mr. Edison himself.

Mr. Edison is too smart a man to waste time trying to find out unnecessary things. "Methinks there is a method in his madness."

CHARLES H. LAWALL.

ORIGINAL PAPERS

PELARGONIUM OIL.

PROFESSOR RICHARD KNUTH,

CHARLOTTENBURG, GERMANY.

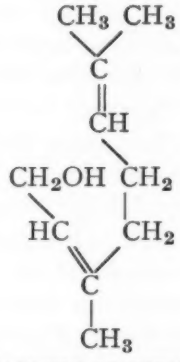
(*Continued From the May Number, Page 315.*)

CHEMICAL CONSTITUTION OF THE PELARGONIUM OIL.

It is probable that the oil was produced first by Recluz, at Lyons, in 1819, by means of steam distillation (*Pharm. Jour.*, London, I, 11, 1852, p. 325). The knowledge of its constitution is, however, the result of the last thirty years. The reason for this is the complicated construction of most of its elements which, like many camphors, stand on the frontier between the acyclic and cyclic hydrocarburets. Up to now there are known to be contained in the pelargonium oil: the alcohols: geraniol, citronellol, linalol, isoamyl-alcohol; a paraffine; the terpenes phellandrene and pinene; a cyclic ketone; the menthone; the terpineol; a blue-colored high-boiling potion, and different paraffine acids.

The geraniol, $C_{10}H_{18}O$ represents the well-redolent part not only of the pelargonium oil, but also of the palmarosa-oil, the true rose-oil, and of many other ètherial oils. Some of the secondary ingredients confer upon the oil the by-odor which distinguishes the pelargonium-oil from the true rose-oil. The geraniol itself was produced artificially for the first time by the firm Schimmel & Co., from the citronella oil. This method was protected by the German Imperial Patent No. 76,435. According to the accounts (Schimmel, Ber., 1894, I, p. 63; 1894, II, p. 77; 1895, I, p. 76), the pure geraniol is a colorless liquid of roseal odor, optically inactive, and with a specific gravity, varying from 0.882 tc 0.885, at a temperature of 15° C. It boils at 230° C. In alcohol it is very easily soluble: in from 12 to 15 parts of a 50 vol.-per cent. alcohol. A disadvantage

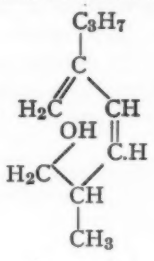
lies in its very easy oxydation, by which its specific qualities are partly changed.



GERANIOL ACCORDING TO TIEMANN AND SEMMLER.

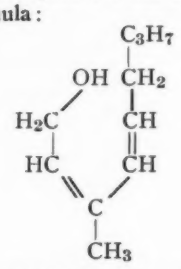
The history of geraniol is rather complicated. It was first pointed out by Jacobsen (Liebig's Ann. Chem., CLVII, 1871, p. 232), in connection with the oil of Andropogon. Later geraniol was found by Gintl (Jahresber. f. Chemie, 1879, p. 941) in the oil of pelargonium. Its constitution was explained by Semmler. Then the active element in the true pelargonium-oil was recognized by Monnet and Barbier (Comptes rendus, CXVII, 1893, pp. 1092-1094), as a specific alcohol of the formula $C_{10}H_{18}O$ and which was identified with the rhodinol of the true rose-oil[1] (Conf. Germ. Imp. Pat. No. 80,007). From both oils they produed, by means of oxydation an aldehyde, the rhodinol $C_{10}H_{16}O$, a tetrasubbromide $C_{10}H_{18}Br_4O$ and a dichlorhydrate $C_{10}H_{18}Cl_2$. Markownikoff and

[1] The name is owing to Eckart (*Chemische Untersuchungen des deutschen und des türkischen Rosenöls,* Inaug. Diss., Breslau, 1891, p. 14). He accepted for his rhodinol the formula:



Reformatski [2] (Journ. prakt. Chem. Ser. 2, Vol. XXXXVIII, 1893, pp. 293-314) thought they had found in the true Bulgarian rose-oil an alcohol of the formula $C_{10}H_{20}O$, the roseol. This roseol of the rose as well as the rhodinol of the pelargonium should be different from the geraniol. For the rhodinol this difference was asserted for a long time by Barbier and Bouveault (Comptes rendus, CXVIII, 1894, pp. 1154-1157). They later gave more exact accounts concerning the constitution of the substance (Comptes rendus, CXIX, 1894, pp. 281-284 and 334-337; CXXII, 1896, pp. 529-531). Hesse (Journ. prakt. Chem., Ser. 2, Vol. L, 1894, pp. 472-479) believed to have found as the principal element of the Réunion oil and of the true German rose-oil, an alcohol, the réuniol, which should be, as well as the true geraniol, the true rhodinol of the French chemists. Erdmann and Huth (Journ. prakt. Chem., Ser. 2, LIII, 1896, pp. 42-46), and Erdmann (Journ. prakt. Chem., Ser. 2, LVI, 1887, pp. 1-47) denied the existence of the réuniol, which they identified with the rhodinol and also believed to be identical with the geraniol of Jacobsen. According to the researches of Bertram and Gildemeister it was finally found by Schimmel (Ber., 1895, I, pp. 37-39; 1896, I,

As Semmler accepted for his alcohol which he had found in the andropogon-oil the formula:



Poleck presumed (Verh. Ges. deutscher Naturforsch. u. Aerzte, LXIV, Vers. II, 1891, p. 77), just as Eckart (*Chem. Untersuchungen des deutschen und des türkischen Rosenöls,* in Ber. Deutsch. Chem. Ges., XXIV, 1891, pp. 4205-4210), that the rhodinol which Eckart had found in the true rose-oil and the geraniol were different. Compare also the previous remark of Poleck (in Ber. Deutsch. Chem. Ges., XXIII, 1890, pp. 3554-3555), in which he was inclined to identify the alcohol of the rose-oil and of the andropogon-oil (the geraniol of Semmler).

[2] Compare also the historical dates of the researches into the true rose-oil.

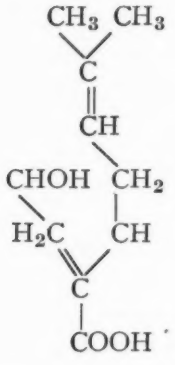
pp. 36-41), that rhodinol, roseol and réuniol had in common the possession of geraniol, to which was added a second alcohol, which later was determined by Wallach (Central Blatt, 1896, I, p. 809) as citronellol. As to the question whether the name of citronellol or rhodinol had the right of priority, there have been many disputes. The name of rhodinol had been claimed also for geraniol by Erdmann and Huth (see above); then by Poleck (Journ. prakt. Chem., Ser. II, LVI, 1897, pp. 515-519). The question had also been decided by Bertram and Gildemeister (Journ. prakt. Chem., Ser. II, LVI, 1897, pp. 506-514). The difficulties connected with the solution of this question may be seen from the following account of the two chemists cited. Rhodinol *Eckart* is a compound of from 20 to 25 per cent. of citronellol with from 75 to 80 per cent. of geraniol; rhodinol *Barbier and Bouveault* is identical with citronellol $C_{10}H_{20}O$; rhodinol *Erdmann and Huth* is identical with geraniol $C_{10}H_{18}O$; rhodinol *Tiemann and Schmidt* corresponds to l-citronellol. Compare besides Bertram and Gildemeister (Journ. prakt. Chem., Ser. II, LIII, 1896, pp. 225-237), and Hesse (*ibid.*, pp. 238-241).

The geraniol was found up to now chiefly in the following oils: essence of acacia-blossoms (Schimmel, Ber., 1903, II, p. 15); essence of champaca-blossoms, prepared from Michelia species (Schimmel, Ber., 1907, II, p. 18); citronellol-oil, from Andropogon nardus L. (Schimmel, Ber., 1893, II, p. 12); citron-petitgrain-oil, from Citrus limonum Risso (Schimmel, Ber., 1905, I, p. 63); eucalyptus-oil, from Eucalyptus macarthuri H. D. et J. H. M. (Schimmel, Ber., 1907, II, p. 36), from Eucalyptus maculata Hook. (Schimmel, Ber., 1893, II, App. 18), from Eucalyptus maculata var. citriodora Hook. (Schimmel, Ber., 1890, p. 20, App. 18); geranium-oil (Gintl, Jahresber. Chem., 1879, p. 941); gingergrass-oil, from Andropogon spec. (Schimmel, Ber., 1904, I, p. 52); lavender-oil (Schimmel, Ber., 1904, I, p. 131); lemongrass-oil, from Andropogon citratus D. C. (Schimmel, Ber., 1894, II, p. 32); linaloa-oil, from Bursera and Ocotea spec. (Schimmel, Ber., 1904, I, p. 131); neroli-oil, from Citrus bigaradia Risso (Tiemann and Semmler, Ber. chem. Ges., XXVI, 1893, p. 271); orange-petitgrain-oil, from Citrus aurantium Risso (Roure-Bertrand Fils, Ber., 1904, II, p. 35); palmarosa-oil, from Cymbogon Martini Stapf (Jacobsen, Ann. d. Chem.,

CLVII, 1871, p. 232); rose-oil, from Rosa damascena Mill. (Bertram and Gildemeister, Journ. prakt. Chem., IL, 1894, p. 184); ylang-ylang-oil, from Anona odoratissima (Reychler in Bull. Soc. chém., III, 1894, p. 1051); Yu-ju-oil, from a lauracea (Nagai in Monopoly Bureau, Government of Formosa 1914, Ref. in Schimmel's Ber., 1915, I, p. 43).

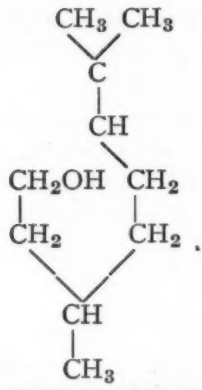
PHYSIOLOGICAL EFFECTS OF THE GERANIOL.

Hildebrandt (Arch. f. experim. Pharm. u. Pathol., XXXXV, 1901, p. 121) injected geraniol into the blood of white mice and noticed already at an injection of 0.05 gr. signs of poisoning. As a product of transformation the same author found in conies a two-basic acid of the melting point of from 192° to 194° C., which may have the formula $C_{10}H_{14}O_4$, and which may be constructed in this way:



The isolation of L.-Citronellol, $C_{10}H_{20}O$, from the pelargonium-oil was accomplished by Tiemann and Schmidt (*Ueber die Verbindungen der Citronellol-reihe,* in Ber. Detsch. chem. Ges., XXIX, 1896, p. 921). It is the left form as also in the true rose-oil. In the true rose-oil its polarization amounted to 4° 20′ in the 1 dm. reed., in the Spanish pelargonium-oil to 1° 12′, in the African to 1° 20′, in the Réunion-oil to 2° 15′.

Linalol, $C_{10}H_{18}O$, akin to the two preceding alcohols, was first identified by the chemists of the firm Schimmel & Co. (Schimmel's Ber., 1904, I, p. 51) in the Réunion-oil. Its boiling point under a pressure of 760 mm. is near 198° and 200° C. The proof of the existence of linalol in Réunion-oil was brought out by the same authors (Schimmel, Ber., 1910, II, p. 51).



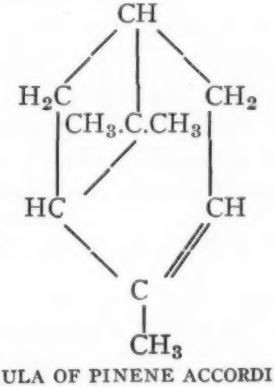
CITRONELLOL ACCORDING TO TIEMANN AND SCHMIDT.

Isoamylalcohol $C_5H_{11}OH$, with one of its isomerics was produced from the first runnings of the distillation of Réunion-oil (Schimmel, Ber., 1904, I, p. 51).

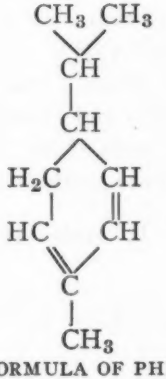
A paraffine was found by Barbier and Bouveault (Compt. Rend. CXIX 1894, p. 281). It was discovered in the remainders of the distillation in the vacuum. It is of crystalline quality and melts near 63° C. Its insolubility in 10 per cent. alcohol permits the conclusion that it is a paraffine.

Phellandrene $C_{10}H_{16}$, a monocyclic terpene. It was identified in the first runnings of Réunion-oil (Schimmel, Ber., 1904, I, p. 51).

Pinene $C_{10}H_{16}$, a bicyclic terpene. It was produced with the preceding from the first runnings of the Réunion-oil (Schimmel, Ber., 1904, I, p. 51).



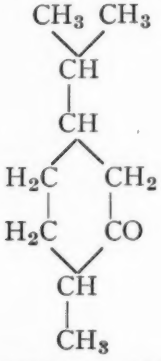
FORMULA OF PINENE ACCORDING TO WAGENER.



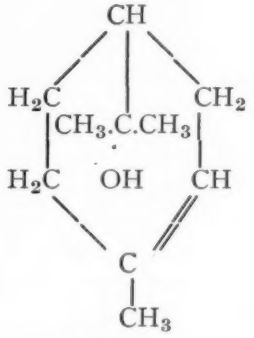
FORMULA OF PHELLANDRENE.

A terpineol $C_{10}H_{18}O$, a tertiary alcohol, was identified and isolated from the Réunion-oil by the chemists of the firm of Schimmel & Co. (Ber., 1910, II, p. 51; 1911, II, 46).

Menthone $C_{10}H_{18}O$, a cyclic ketone, was first found by Flatau and Labbé (Bull. Soc. chim., Paris, Ser. 3, XIX, 1898, pp. 788-790), then by the chemists of the firm Schimmel (Ber., 1904, I, p. 50), in the first runnings of the distillation, and in great quantity.



MENTHONE ACCORDING TO BECKMANN.



TERPINEOL.

A blue-colored high-boiling potion, as it exists in many etheric oils, is found also in the pelargonium-oil. Its composition is unknown. Probably it is the cause of the bluish-greenish color of the Réunion-oil. (Semmler, *Aetherische Oele,* III, 1906, p. 262.) Barbier and Bouveault were the first to call attention to it. They determined the boiling-point between 165° and 170° C., under a pressure of 10 mm.. In their opinion it is perhaps an ether of the formula $(C_{10}H_{17})_2O$.

Ester of geraniol and citronellol. The knowledge of this body is due to Barbier and Bouveault (Compt. Rend., CXIX, 1894, p. 281; cf. also the travels of the firm Schimmel & Co., Ber., 1894, I, p. 31). Both alcohols are partly bound to the following acids: a. Acetic acid, CH_3COOH. b. Isobutyric acid $\rangle$ $CH.COOH$. c. Isovaleric acid $\rangle$ $CH.CH_2.COOH$. d. Tiglinic acid $CH_3\text{-}CH{=}C(CH_3)\text{-}COOH$. e. An

acid of the boiling-point at 250° C., which has probably the formula $C_9H_{15}COOH$.

In the Réunion-oil there are ester-contents of about 31 per cent.; in the Algerian oil, 29.1 per cent.; in the Spanish oil, 23.7 per cent.

The occurrence of pelargonium-acid in pelargonium-oil is very doubtful, though Pless (Semmler, *Aether. Oele,* I, 1906, p. 766) believed to have found it there, and though it is also indicated by Gintl (Zeitschr. allgem. Oesterr. Apoth. Ver., XVII, 1879, p. 268). Charabot and Gatin (Journ. d'Alger. Inp., XVII, 1913, p. 290) also named citral $C_{10}H_{16}O$, an aldehyde, which is distinguished from geraniol by the possession of COH instead of CH_2OH in the final member. That substance had been isolated from the true rose-oil, but it is not known to me, whether it has been found in the pelargonium-oil.

DIFFERENCES IN THE COMPOSITION OF THE PELARGONIUM-OIL ACCORDING TO ITS ORIGIN.

According to Charabot (Bull. Soc. chim. sér. 3, XVII, 1897, pp. 489-492), the pelargonium-oil differs from the palmarosa-oil by the existence of active esters. He has shown that by addition of an alcoholic caustic lye polarization decreases in the pelargonium-oil, but not in the palmarosa-oil, which proves that the latter does not contain active esters. His experiments referring to the pelargonium-oil are found in the following table:

Origin of the oil.	Contents of geranyl-tiglinate.	Alcohol $C_{10}H_{18}O$	Total alcohol.	Specific gravity at 15° C.	Power of polarization l-100 mm.	Power of polarization after saponification.	Decrease of the power of polarization.
Algeria, 1895,	25.31%	46.22%	62.74%	.896	—9° 50′	—5° 46′	4° 4′
Algeria, 1895,	22.11	50.80	65.23	.899	—9° 20′	—4° 24′	4° 56′
Algeria, 1896,	23.32	60.30	75.52	1.898	—9° 48′	—5° 46′	4° 2′
Algeria, 1896,	25.66	41.80	58.55	.895	—10° 4′	—5°	5° 4′
Algeria, 1896,	24.86	55.41	71.62	.894	—9° 10′	—5° 8′	4° 2′
Réunion,	32.16	46.12	67.11	.8915	—9° 20′	—7° 40′	1° 40′

According to these figures the Réunion-oil rather differs from the Algerian oil.

Tiemann and Semmler (Ber. deutsch. chem. Ges., XXIX, 1896, p. 924), indicate the following differences:

Contents of Alcohol.

Spain,	70 p. c.	65 p. c. geraniol,	35 p. c. cit.
Algeria,	75 "	80 " "	20 " "
Réunion,	80 "	50 " "	50 " "

Cf. also the account of the chemists of the firm Schimmel & Co., Ber., 1897, I, Anh., 23.

	Spec. gravity at 15° C.	*Power of polarization in 100 mm. canc.*	*Contents of esters calculated in geranyltiglinate.*
Algeria,	0.892-0.9	6°30′-10° (1)	19-29 p. c.
France,	0.897-0.905	7°30′-9°30′ (1)	25.28 "
Réunion,	0.889-0.893	8°-11° (1)	27-33 "

An analysis of Simmens (*Pharmac. Journ.*, XCI, 1913, p. 143) indicates the following values of geraniol and citronellol for the different oils:

	Total-geraniol.	*Citronellol*
Algeria,	69.3-79.5 p. c.	32-43 p. c.
Réunion,	69.7-73 "	44-51 "
Corsica,	69.8 "	30.3 "

Another account (*Perfum. Record,* IV, 1913, p. 328, says that by the methods of acetic acid and formic acid the following values had been found in six different geranium-oils, of which, however, the two last must be referred to cymbogon species.

	Total-geraniol.	*Citronellol.*
France,	72.7 p. c.	39.8 p. c.
Algeria,	74.1 "	32.9 "
Réunion,	73 "	44.3 "
Corsica,	73.3 "	45.9 "
Asia,	72.1 "	51 "
Asia,	69.1 "	62.3 "

The analysis of the pelargonium-oil which has been produced in Sicily gave, according to Umney and Bennet (*Pharm. Journal,* LXXV, 1905, p. 860; *Chemist and Druggist,* LXVII, 1905, p. 970), the following results: Geranyltiglinate 35.6 per cent., total-geraniol 71.9 per cent. The contents of esters were greater than in French and Algerian oils and almost equaled those which had been observed in Réunion-oil.

ALTERATIONS OF THE CHEMICAL COMPOSITION OF THE OIL THROUGH CHANGE OF WEATHER.

Charabot (Bull. Soc. chém., sér. 3, XXIII, 1900, pp. 922-928) examined two oils, which had been produced on July 18th and August 21st. The examination showed that specific gravity, polarization and contents of esters showed an increase, the contents of free acids and free alcohols, however, a decrease. The total contents of alcoholic components, however, was greater in the latter case. The quantity of citronellol seemed, according to Charabot, to be greater in proportion to geraniol. According to Jeancard and Satie (Bull. Soc. chim., sér. 3, XXXI, 1904, pp. 43-49), cold nights reduce the contents of alcohol. This decrease is, however, not the result of an intensive production of esters, but only to a decrease of oil. The contents of geraniol becomes smaller, that of citronellol increases in proportion to geraniol. While in many other oils, such as the neroli- and the petitgrain-oil the decrease of free alcohols is compensated by a greater production of esters, here the loss touches only the geraniol, whereas the citronellol increases slightly.

FALSIFICATION OF PELARGONIUM-OIL BY MODERATE CHEMICAL DRUGS.

In most cases they can be recognized by the odor; but often they imitate well the weight of the oil. In literature there are found accounts of falsification by means of the following substances:

Dimethylsulphide (Schimmel, Ber., 1909, I, p. 50); Aethyloxalate (*Perfum. Record,* 1911, II, p. 83); diphenylmethane (Charabot and Gatin, Journ. d'Agric. trop. XIII, 1913, p. 294); ester of benzoic-acid (Schimmel, Ber., 1905, II, p. 33); Aethylphthalate up to 20 per cent. (Schimmel, Ber., 1913, I, pp. 59-60); gurjunbalsam-oil, the oil of an East-Indian Dipterocarpus, up to 30 per cent. (Schimmel, Ber., 1908, I, p. 53; 1911, II, p. 47); derivates of the lemon-oil (Charabot and Gatin, l. c., p. 294).

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COMPARATIVE RESEARCHES ON THE METHODS PROPOSED FOR THE ESTIMATION OF GLYCYRRHIZIN IN LICORICE ROOT AND IN LICORICE EXTRACT.

By Armin Linz.

(*Prize Research of the Hagen-Bucholz Foundation, 1913-1914.*)
(*Archiv der Pharmazie,* 1916, Vol. 254, 65-134, and 204-224.)

TRANSLATED BY DR. PERCY A. HOUSEMAN. APRIL, 1921.

For a long time past, workers have concerned themselves with a large numer of researches and publications on the constituents of licorice root and extract. As early as about 1800, Pfaff, Hermbstädt and Schwartze published statements on the composition of licorice root and extract, and also made known the characteristic precipitates which various reagents produced with an infusion. In the succeeding decades, the literature on this subject attained a considerable volume. All of these researches, however, up to about 1880, propose only the isolation of the characteristic ingredient of the root and extract, without placing any emphasis on a quantitative determination of it. Although for this reason, the above-mentioned researches have no direct connection with the methods used for the determination of glycyrrhizin, still I deem it necessary to give a survey of them. In the first place, there is naturally a certain dependency between the first experiments for the isolation of a substance and its quantitative determination; further, such a summary, taking into consideration all the papers which have appeared, has not hitherto been attempted.[1] The short summaries which precede the researches of Tschirch, Rasenak, Cederberg and Gauchmann, are incomplete, and are also partly erroneous.

In Appendix A is given a list of all the researches which are concerned with the ingredients of licorice root and extract, their chemistry and their quantitative examination. The claim may be made for this collection that it takes account of all the more im-

[1] The contents of these publications are given in the original dissertation in adequate fashion. At this time, however, it will suffice to communicate the author's results concerning the quantitative examination of licorice extract and root, and for the rest, to refer to the bibliography in Appendix A.—The Editor.

portant work published on this subject. Such a list has not been given before. The reviews in the older works such as Flückiger's "Pharmakognosie," Husemann's "Pflanzenstoffe," Tschirch's "Handbuch der Pharmakognozie," Dragendorff's "Die Heilpflanze," and Wehmer's "Pflanzenstoffe," are far from complete. Further, since the "Jahresbericht der Pharmazie" has not noted all of the articles, it was only possible to make such a list after examining all of the journals concerned.

Through the kind offices of several gentlemen, it was possible for me to examine nearly all of the articles in the original. I was also able to work on nearly all of the original articles in foreign journals, thanks to the use of the journal catalog of the "Auskunftsstelle deutscher Bibliotheken" now in the press, as well as the use of the library of the "Deutschen Apotheker-Vereins," and of the "Reichsgesundheitsamtes." In the case of those publications which I could not see in the original, I have used those abstracts which were available to me.

The Quantitative Determination of Glycyrrhizin in Licorice.

The idea of determining the glycyrrhizin content, and of using it for the evaluation of licorice, belongs to Rump. As I have already indicated, he made the following statement in 1855: "The value of licorice is best determined from its content of glycyrrhizin, as is that of opium from its content of morphine." This statement did not remain uncontradicted. Shortly afterwards, Hager claimed the contrary. In spite of that, however, he stated there should be at least 10 per cent. glycyrrhizin in licorice extract. The next decades brought forth a large number of proposals for the quantitaive determination of glycyrrhizin, from which it must be deduced that this determination was of value for determining the quality of any variety of licorice. In later years, however, more attention has been given to the sugar determination. This is justified. Outside of the obvious estimations of the soluble and insoluble portions, and of the ash, the determinations of glycyrrhizic acid and sugars are indispensable for a correct valuation. For example, by determining the glycyrrhizin alone, one could not detect the frequently-occurring adulteration with sugar, of an extract containing much glycyrrhizin. For this reason many of the later workers on this subject have taken up determination of sugars. I would only name here Houseman, Telle, Parry, Tschirch, etc.

A chronological list of the methods of glycyrrhizin determination published to date is collected at the close of this article under Appendix B.

A number of proposed methods, particularly those given in general works, are taken in part from other sources and appear, sometimes under other names, as original determinations. I found, for example, the method proposed by Diehl, under the name of Prollius in Hager-Fischer-Hartwich's "Handbuch der Pharmazeutischen Praxis," 1896. Hager's Handbuch has the method of Haffner in the supplementary volume. König's "Nahrungs und Genussmittel," 1, p. 1065, has reproduced the method of Kremel.

In the list in Appendix B I have only included original methods.

One can see how the glycyrrhizin content of licorice varies with the large number of quantitative methods employed. Glücksmann found in one kind of licorice, no glycyrrhizic acid at all, and others claimed to have found amounts up to nearly 30 per cent. Not only in different kinds, but also in the same kind at different times, have large variations in the glycyrrhizin content been found, a fact which finds its explanation in the very primitive methods of manufacture which are even yet partly used. The desire, which has often been expressed, to establish in the Pharmacopœia a lower limit for the glycyrrhizin content, or to describe the preparation in the Pharmacopœia regulations, is justified on these grounds.

From the very few comparisons of different methods hitherto available, it is to be seen that, by the many methods proposed, results differing largely from each other are obtained. I would here quote Erikson, who obtained 16.5 per cent. and Cederberg, 14.3 per cent. glycyrrhizin, even from the same extract. Glücksmann obtained 8 per cent. ammonium-glycyrrhizinate from an ammoniacal extract, and only 2 per cent. from an aqueous extract. Haffner, using Helfenberg's method, obtained 4.3 per cent., Kremel's method 3.1 per cent., and Diehl's method 6.4 per cent., using the same licorice extract for all. Haffner has compiled interesting tables in which he believes he demonstrates a connection between the extraction liquid, the method of purification, and the degree of purity of the glycyrrhizic acid obtained and weighed.

These results, which are so poorly comparable, justify the conclusions that the question of the method of glycyrrhizin determination is not yet cleared up. This fact, combined with the necessity of

such a determination, gives to the Foundation Research of this year great practical value.

Various workers in this province have designated as "thankless," their activities with glycyrrhizin, not only in the matter of ultimate analysis, but also from a quantitative-analytical point of view. This is easily understood, particularly in the latter respect. A pure glycyrrhizin, or an equivalent compound, can, in my opinion, not yet be obtained quantitatively. One only obtains a more or less impure acid or derivative, with varying losses.

INTRODUCTION TO QUANTITATIVE DETERMINATIONS.

Before I enter into control experiments of the individual methods proposed, and the results obtained, I should like to discuss here some fundamental questions which are of common importance to all or many of the methods proposed. I think I can, by this means, avoid unnnecessary repetition.

In the first place may be mentioned the influence of the liquid which is used as a solvent for the licorice extract. Further, account should be taken of the acid used for precipitation. Then, the solubility of the glycyrrhizic acid in the precipitant, and in water, and the resultant losses must be investigated. And, finally, account must be taken of the degree of purity of the substance weighed. As regards the many questions which apply only to individual determinations, I shall consider these under the respective methods.

1. *The Liquid Used to Dissolve the Licorice Extract.*—The first proposals are, naturally, to dissolve the licorice in water, but it was found that this solution is extremely difficult to filter. In order to avoid this trouble, Diehl proposed, in 1883, to add an equal volume of alcohol after dissolving in water, and then to filter after settling. It is interesting that Diehl emphasized this proposal, on the ground of the easier filtration achieved. However, he not only achieved this practical object, but also obtained a greater purity in the acid which is separated later. By the addition of alcohol, the gummy and mucilaginous substances, which are present in considerable quantity, and which would otherwise pass into the filtrate, are precipitated. In the subsequent precipitation, one also naturally obtains a purer glycyrrhizic acid. In any case, the addition of alcohol to the aqueous extract must be regarded as an improvement, especially since no loss

of glycyrrhizin can, in general, occur. Under these circumstances, it is remarkable that since Diehl, and also quite recently, methods have been published which use no alcohol. The latter are, without doubt, inferior to those using alcohol.

Rump in 1855 appears to have been the first to propose an ammoniacal solvent for licorice extract. As I already mentioned in the introduction, he deduced, from the fact that the matters insoluble in cold water yielded a certain amount to ammonia, that there was present a glycyrrhizin soluble in water, and one soluble only in ammonia. Schroeder also, in 1883, emphasizes the difference between soluble and insoluble glycyrrhizin. I consider this ammoniacal extraction not the correct method.

In the introduction, I have mentioned that Tschirch considers the "glycyrrhizin" of the root present as a potassium and calcium salt of glycyrrhizic acid. He arrived at this view on the basis of the following experiment: A saturated aqueous infusion of the root was treated with an equal volume of alcohol, filtered, and to the filtrate three times the volume of absolute alcohol added. The glycyrrhizin compounds were thus precipitated. The precipitate was filtered off, dissolved in glacial acetic acid, and purified by crystallization. Tschirch obtained two kinds of crystals, which showed by qualitative analysis, the presence of potassium and calcium.

The statement of Flückiger in 1867, that "glycyrrhizin" is the ammonium salt of the acid, has been doubted by many, among them Sestini. Tschirch considerd that he has definitely disproved this view, since in the precipitate mentioned above, he found no ammonium compound. The opinion which has been published in one paper, that the magnesium salt of the acid is concerned, is in itself not improbable. It has, up to the present, not been contradicted. In addition to the combined acid, the root is said to contain, according to statements in the literature which agree on this point, also small quantities of free glycyrrhizic acid.

In the preparation of licorice extract, which is, in part, still very primitive (see Tschirch's "Handbook" and Anselmino-Gilg "Commentary"), the root is boiled with water. The small quantities of the free acid are certainly neutralized by the constituents of the well-water, or by salts of the root, so that it may be taken as established, that glycyrrhizic acid occurs in licorice extract only in combined form. Without wishing to decide the question of what compounds

are present in the extract, I will here only consider the possibility that it can be a question of a potassium, calcium, magnesium, and ammonium salt. The potassium and ammonium compounds are very easily soluble in water. The literature says nothing about the magnesium compound, which does not appear to have been prepared yet. It may, however, be assumed from the nature of magnesium salts, that the glycyrrhizinate is easily soluble. As regards the calcium salt, Sestini reports that it is difficultly soluble in water. When one remembers, however, that by the various methods, only very trifling quantities of calcium salt are present to be dissolved, one may assume that the calcium glycyrrhizinate will be dissolved in the amount of water used in the determinations.

All possible compounds present in licorice extract as "glycyrrhizin" are therefore water-soluble for the purposes of our practical testing comparisons. A free acid which must be made soluble by alkali, is not present. It is therefore superfluous to add ammonia to the solvent. Such an addition is not only unnecessary, but even undesirable, for Haffner has proved that calcium glycyrrhizinate is extremely difficultly soluble in ammonia. There is another important fact which argues against such an extraction. It is proved that ammonia dissolves a considerable quantity from the residue insoluble in water. If it be possible to dissolve out with water the total glycyrrhizic acid compounds (and I am of the opinion that this can be done, provided, of course, that not too small quantities of water are used), then it is incorrect to use ammonia, and thus extract still more from the otherwise insoluble matter, which does not contain glycyrrhizin compounds. The more "non-glycyrrhizin" the filtered extract contains, the more impure must the precipitated glycyrrhizic acid be. Or, positively stated: The precipitated glycyrrhizic acid is the purer, the greater the insoluble residue, presuming, of course, that the total glycyrrhizin compounds have been extracted from it. I will merely mention that an ammoniacal licorice extract is appreciably more difficult to filter than an aqueous extract. The above remarks explain why I obtain higher values in using ammoniacal extracts, than in using pure water in the control experiments to be discussed later. This excess is, however, only obtained at the cost of the purity of the weighed product. For all of these reasons I hold an ammoniacal treatment of the original licorice extract to be incorrect.

As a third extraction-liquid, Haffner proposes a mixture of sulphuric acid and alcohol. Alcohol alone dissolves practically nothing from licorice extract, since all of the glycyrrhizin compounds are very difficultly soluble or almost insoluble in alcohol. By the addition of sulphuric acid, the glycyrrhizin compound is decomposed, and the free glycyrrhizic acid is formed, which is easily soluble in the mixture of alcohol and sulphuric acid. Haffner, therefore, avoids the question of the solubility of the various compounds, by setting free the glycyrrhizic acid. The question as to whether this treatment dissolves out all of the glycyrrhizin, I can answer unconditionally in the affirmative. It can hardly be doubted that the total glycyrrhizin salts of licorice are decomposed by sulphuric acid or that the free glycyrrhizic acid so liberated is soluble in the sulphuric acid-alcohol mixture. There is therefore no objection to Haffner's proposal from a quantitative point of view.

In order to determine whether there is anything soluble in ammonia in the dry residue from Haffner's method, I extracted exactly 5 grams of the insoluble matter with ammoniacal water. Even after the third extract, the decanted liquid was quite black. From the united evaporated extracts, I was able to obtain 0.189 grams ammonium glycyrrhizinate in the usual analytical way. Since this 5 grams residue corresponds to about 10 grams of original licorice extract, there is found by this method, in the residue from Haffner's method, nearly 2 per cent. of "ammoniated glycyrrhizin" which contains no glycyrrhizic acid, but which, by an ammoniacal extract of licorice would probably be obtained as an impurity in the acid, and would be weighed as glycyrrhizic acid.

I would, therefore, state my opinion on the various proposed extraction-liquids as follows: Both the aqueous extract followed by alcohol, and also the alcohol-sulphuric acid extract, give good results; but, on the contrary, the ammoniacal extract is inferior to both, because it gives values which are higher than the correct figure.

2. The Solubility of Glycyrrhizic Acid.—As far as I could determine, Haffner, in 1899, was the first to make experiments on the solubility of glycyrrhizic acid. Maisch, in 1884, in commenting on the method proposed by Schroeder, showed, that such a solubility determination is very desirable. Haffner shook up glycyrrhizic acid with excess of water, and determined the solubility by evaporation. He found the proportion 1 : 60, which corresponds to 1.67 per cent.

He emphasizes particularly, that he did not make this experiment with pure acid, for the reason that such a substance is not obtained in the quantitative determination. Capin in his dissertation, made detailed researches on the solubility determination, but the conclusions which he drew are partly incorrect. I will here only consider his solubility determinations. I will speak of their application to his proposed method of determining glycyrrhizic acid when I discuss that subject.

When one adds sulphuric acid to precipitate an extract of licorice or a glycyrrhizin solution, the supernatant liquid remains colored. From this Capin concludes: "If now the total glycyrrhizic acid had been precipitated by the addition of sulphuric acid, it is evident that the liquid, after filtration, would not show the least color." This conclusion is incomprehensible. It would be true, and only then conditionally, if pure glycyrrhizic acid were colored, or better, black. But Capin has written the above statement in spite of having read the researches of Tschirch! In order to determine its solubility, Capin shakes up 25 grams glycyrrhizic acid (impure, washed with water, alcohol and ether) with 200 cc. water, and allows the liquid to stand for 24 hours. He then filters, and cools the clear solution to 0° in a mixture of ice and salt. A further precipitate is formed, which is filtered off through a funnel kept at 0°. He then dries 20 cc. of this filtrate to constant weight, and obtains 0.110 grams of residue which corresponds to a content of 0.55 per cent. (not 0.575 per cent., as is stated in Capin's dissertation in consequence of a misprint). Under the same experimental conditions, he then determines that the solubility factor at 15° amounts to 0.575 per cent. These two numbers, as shown above, have become mixed, and the error has been carried into the French journals in part, for example, in the *Repertoire de Pharmacie*, III, 24, p. 14. In consequence of this error, Anquet has called the attention of the author to the unusual procedure in prescribing a temperature of 0° although the solubility according to his results, is higher at 0° than at 15°. A comparison of the dissertation with the Bulletin des Travaux de la Société pharmaceutique de Bordeaux shows at once that it is only a question of an oversight or a printer's error. The conclusions of Anquet are therefore not justified.

The observation of Capin, that a clear solution, from which the glycyrrhizin has been precipitated, separates a further quantity of the

acid by cooling to 0°, is confirmed by myself. I noticed it particularly in the method of Evans' Sons, which will be treated later. It may, therefore, be taken as proved by this simple experiment, that glycyrrhizic acid is less soluble in water at 0° than at 15°, from which one deduces the obvious application to the analytical method. A similar method for determining the losses in the glycyrrhizin determination, due to the solubility of the acid in water, is described by Durier.

He dissolves the glycyrrhizic acid, which he had precipitated in previous experiments, in 25 cc. water, and precipitates with hydrochloric acid. He filters and weighs the residue. The difference between glycyrrhizic acid used, and that finally weighed is considered by him as the solubility number in 25 cc. of water. Here also an error is involved. Durier does not determine the solubility in water, but in acidified water. These two solubility numbers are entirely different! In discussing Durier's work I shall go into this in detail.

We see that Haffner, Durier and Capin have concerned themselves with the solubility of glycyrrhizic acid, and that all three, under different experimental conditions, arrived at quite different results. Under these circumstances the question presents itself: Have these experiments any object? Theoretically it must be obviously answered in the affirmative, but it is otherwise with the practical side of this question as regards the application for the present work. First of all the question must be answered: Shall the solubility of the chemically pure or of the impure acid be investigated? Haffner voices his views as follows: "Chemically pure acid does not enter into the practical question, therefore for the solubility determination I use the impure acid." I am of the same opinion. Nobody has yet succeeded, and in my opinion never will succeed, in weighing approximately pure glycyrrhizic acid quantitatively. I therefore consider it of no practical value to determine how much of the pure acid dissolves in water, since one always works with impure acid. One always weighs "glycyrrhizin plus impurity." Of this mixture the pure acid, or the impurity, or a portion of both may dissolve in water. Since one weighs the impure acid it would be inaccurate to take into account only the solubility of one constituent of the mixture of glycyrrhizic acid plus impurity, and to neglect that of the other. Judging from this line of thought, one should determine the solubil-

ity of the impure acid. But here one encounters manifold difficulties in its accomplishment.

Haffner, Capin and Durier were each working with different materials. It is therefore necessary to take into account the degree of purity or impurity. It would not be fair to judge the results of an experiment on one acid from the results on other acids. If one wishes to obtain exact results and to add the percentage solubility to the value found in a glycyrrhizin determination, one would have to do a solubility determination for every kind of glycyrrhizin determintion. In that case it would be necessary to dry the glycyrrhizin at a 100° to constancy, which treatment would undoubtedly change its physical properties. I would only quote one example—the change in its solubility in alcohol, if one dries glycyrrhizic acid at room temperature. It would be unreasonable to assume that the washing of the precipitated wet acid entails the same losses as result from the use of the completely dried acid. In spite of this, it has been proposed to compare these results!

The attempt which Capin and Durier have made, to correct for the losses due to washing in the respective analytical procedures, by the addition of a number to the glycyrrhizin value obtained, which shall be valid for all kinds of licorice is, in both cases, not only inapplicable on account of inaccurate experimental conditions which result from the solubility determination, but is also open to fundamental objections. The values which both have found, refer, naturally, only to saturated solutions, which, however never come into question in a glycyrrhizin determination. In the latter case, it is a question only of washing the precipitated acid with water, and of the solubility of the same in the acidified liquid in contact with it. It is, therefore, quite clear that totally different conditions exist, and that they cannot be compared with one another. The experiment of Capin and Durier will therefore never be suitable for quantitative work. A different method which I will mention below might be more applicable.

Summarizing, I would therefore state:

1. It is of no value for the practical glycyrrhizin determination to determine the solubility of the pure acid.

2. A determination of the solubility of the impure glycyrrhizic acid cannot be carried out under conditions which are equivalent or similar to those of a glycyrrhizin determination.

If then the quantitative solubility values seem to have no value, it becomes all the more important to establish the following facts:

Glycyrrhizic acid is only very slightly soluble in water, and less so in water of 0° than at 15°.

Glycyrrhizic acid is also somewhat soluble in acidified water, but noticeably less so than in pure water.

3. Experiments to Establish Quantitatively the Losses Caused by the Solubility of Glycyrrhizic Acid.—The only procedure which has up to now attempted to establish in a glycyrrhizin determination, the losses due to solubility, and to give a figure for them is that of Cornimboeuf. I will discuss it at this place since Cornimboeuf only treats of the estimation of glycyrrhizic acid in ammoniated glycyrrhizin, which is not the purpose of this work. Cornimboeuf filters the glycyrrhizin which has been precipitated with sulphuric acid, and dissolves it in ammonia. He evaporates the supernatant liquid, together with the wash waters almost to dryness, kneads the tough black residue successively with 10, 10, and 5 cc. of water, filters the wash water, dissolves the remaining second portion of glycyrrhizic acid in ammonia, unites the two ammoniacal glycyrrhizic solutions and drys them to constant weight. I do not consider this procedure free from objection.

Independently of Cornimboeuf, but in a similar way, I have often attempted to determine at least approximately, the quantitative losses of glycyrrhizin, but I always made the same observation. As the evaporation of the mother liquid and the wash waters progressed, the glycyrrhizic acid separated out at first in brown flakes, which in the course of further evaporation became deep black. They proved to be very difficultly soluble, and partly quite insoluble in ammonia. When one remembers that during evaporation, the water is volatilized, but not the sulphuric acid used for precipitation, and that at the end the glycyrrhizin in the mixture is in solution in a very strong sulphuric acid, one has a sufficient explanation for this condition. Under the influence of the strong acid, decomposition has taken place, and partial carbonization will occur, especially when the evaporation is carried almost to dryness according to Cornimboeuf's method.

Naturally the kneading of the sticky acid with 25 cc. water also causes losses, but unfortunately such losses cannot be avoided in the glycyrrhizin determination.

I have found a different way, which in my opinion is suitable to determine, fairly accurately, the losses in glycyrrhizic acid.

I evaporate the mother liquor and wash waters to a syrup after saturating the free acid with ammonia. I transfer this saturated solution of ammonium glycyrrhizinate, and ammonium sulphate or chloride, to a narrow glass cylinder graduated in ½ ccs. The solution is then brought to such a volume, that for every gram of licorice extract taken, four grams of solution result. I then precipitate the glycyrrhizic acid with sulphuric acid, of which for every gram of acid I used ten drops. After standing twelve hours, the liquor was filtered through a fluted filter, 5 cm. diameter, the acid was collected on the filter paper and washed with 2 per cent. sulphuric acid at 2° C. For this purpose I used 5 to 10 cc., according to the quantity of the precipitate, which is then washed with 5 to 10 cc. of water saturated with ether at 2° C., and the residue is dried over sulphuric acid in a vacuum desiccator. The filter is then extracted with hot 95 per cent. alcohol, the alcoholic solution is evaporated, and the residue weighed as glycyrrhizic acid. By my process I have excluded the possibility of decomposition. Ammonium glycyrrhizinate is so stable that it stands evaporation even to dryness. It is unfortunately not possible to avoid losses, through solubility in the supernatant liquid from the precipitation, but they are quite small. The washing of the glycyrrhizic acid also causes losses, but these are likewise quite small. By following the above experimental procedure I believe that I have obtained practical quantitative results which are interesting in showing the losses sustained by the individual methods.

4. The Acid Used for Precipitation.—Glycyrrhizic acid is a weak acid, which is precipitated by most other acids. For the quantitative determination of glycyrrhizin, it is naturally of value to know which acid is the most suitable for precipitation. The precipitants used in the methods to be investigated are sulphuric acid, hydrochloric, and absolute alcohol. I made comparative investigations with sulphuric, hydrochloric, boric, oxalic, tartaric, phosphoric and formic acids. I made such a solution of licorice that after filtering, the soluble portion of the licorice was present in the proportion 1 : 9. Of this solution 10-gram portions were treated, in wide test tubes, with 2.0 cc. dilute sulphuric acid, 3.0 dilute hydrochloric acid, 5.0 phosphoric, 15.0 hot saturated boric, 15.0 tartaric (5 per cent.), 3.0 nitric, 10.0 formic. The contents of each tube was made up to 25.0 cc. By

a control experiment beforehand, I had convinced myself that the quantities used for precipitation were sufficient. After standing 24 hours, and filtering, these control experiments gave no further precipitate when more of the same precipitant was added. The liquids were filtered after standing 24 hours. The tartaric acid had gelatinized the contents of the tube, so that one could turn it upside down without anything running out. Therefore, it cannot be used for precipitating any better than acetic acid, in which glycyrrhizic acid is easily soluble. The colors of the filtrates, and also that of the precipitated acid, show great variability. The filtrates from boric and phosphoric acid precipitations were light brown; those from sulphuric, hydrochloric and nitric acid, more or less dark brown to black. The precipitated acid was black and uninviting, except with oxalic acid, in which case it had a light grey color, which may be ascribed, probably, to the precipitated calcium salt. To each of the clear filtrates, I then added 2 cc. dilute sulphuric acid. After standing for 10 hours, it was found that all of the solutions, with the exception of the sulphuric and hydrochloric, had precipitated some more glycyrrhizin. The amount of additional precipitate was only slight in the case of phosphoric acid, nitric acid, and oxalic acid, but was considerable in the case of boric and formic acids. Reaction between the first precipitant and the small quantity of dilute sulphuric acid need not be feared, and is not concerned in the precipitation. I arrived at the same conclusions through a second experiment. I prepared a purified glycyrrhizic acid from an alcoholic extraction of the dried acid, and shook up with water, a larger quantity than could be dissolved. To 20 cc. portions of the clear filtrate in large test tubes I added 2 cc. of various acids. Sulphuric, hydrochloric and phosphoric acids gave a turbidity immediately, oxalic and nitric acids only after some time and finally formic acid also gave a trifling turbidity. The liquid was filtered after 24 hours, and on adding 2 cc. sulphuric acid to the still more dilute glycyrrhizin filtrate, after standing 10 hours a flocculent precipitate was formed in all of the solutions, with the exception of those containing hydrochloric and sulphuric acids. From these two simple experiments only one conclusion is possible: Sulphuric and hydrochloric acids react more sharply than other precipitants. In order to decide which of these two acids works the more strongly I proceeded as follows:

A saturated solution of glycyrrhizic acid was diluted, in one case,

with twice, and in another case, with three times the volume of water, and to 10 cc. portions of these solutions were added 1 cc. dilute sulphuric, and 1 cc. dilute hydrochloric acid. After several hours, all four test tubes showed light flocculent, gelatinous precipitates. From another saturated solution, in order to avoid possible decomposition, I made a dilution in the proportion of 1 : 2½, and added to each 10 cc., 1 cc. of the acids. This time, the hydrochloric acid solution remained quite clear, even after 24 hours, while the sulphuric acid solution gave a very light, but positive turbidity. This proves that sulphuric acid unquestionably precipitates glycyrrhizic acid quantitatively, better than hydrochloric, and that the glycyrrhizin is more difficultly soluble in the former than in the latter. Sulphuric acid is therefore certainly the most suitable acid for precipitation. In these experiments, I have intentionally avoided any quantitative determination, since it is here a question of only very small quantities of a material which is not uniform. Under these circumstances, differences in the third decimal place can hardly have any significance. I believe, however, that for practical purposes of a glycyrrhizin determination my two experiments are sufficiently convincing. From them may be stated that only sulphuric and hydrochloric acids may be considered as precipitants, and that the first acid works more exactly and sharply. All other acids cannot be used.

5. *Experiments to Establish the Purity of the Acid Weighed.*— Since, by the various determinations, acids or salts of various degrees of purity are weighed, it is not sufficient, in criticising glycyrrhizin determinations, to compare the quantities obtained and weighed. Account must also be taken of the purity of the same. The only attempt to do this has been made by Haffner. He prepares the barium salt, and determines the barium by evaporation with sulphuric acid, weighing the barium sulphate, and has in this manner a method for determining the purity of the glycyrrhizic acid. If I would now attempt, in the present work, to determine the degree of purity of the acid, I could not, of course, at once accept Haffner's methods. Haffner's acetone extracts have for their object a purification of the acid which is quite foreign to my intention, and in this case would be quite inaccurate. I tried all kinds of variations of Haffner's procedure without attaining my object. I should like, first of all, to mention a few facts established in this connection. A filtered solu-

tion of ammonium glycyrrhizinate leaves an insoluble residue, after it has been evaporated, dried at a 100°, and taken up in water again. Ammonium glycyrrhizinate which had been dried at 100° (as it is weighed), cannot, without purification, be converted to the barium salt. Glycyrrhizic acid dried at 100° cannot be redissolved in 95 per cent. alcohol without leaving a residue. Glycyrrhizic acid itself cannot be converted to the barium salt without purification. In the barium salt obtained, the barium could be determined, and from that, an indication of the purity of the salt could be obtained. But this does not result in even an approximate estimate of the purity or impurity of the acid or ammonium salt weighed. To all these facts and thoughts can be added the same objections made against the purity test of Haffner's.

I therefore come to the conclusion that it is not possible, according to Haffner's proposal, or any other methods, to determine the degree of purity of the acid, even approximately. I cannot accept the degrees of purity set up by Haffner for the various acids. According to his own results, he can hardly accept them—and if he does, they do not give a true picture—and he offers no other method. Although such an exact determination of the degree of purity is very desirable and indispensable for a conclusive estimate of the individual methods proposed, one is left to rely only on the taste and appearance as a measure of control. It is shown that the ammoniacal extract undoubtedly gives a less pure acid than an aqueous extract, and for the same reason the use of alcohol is to be preferred to a purely aqueous solution. From the appearance of the acid weighed, it is to be seen that a purification with alcohol according to Diehl is important. The ammonium glycyrrhizinate obtained by Diehl's procedure is of a light brown color, while that from the other methods is colored dark brown.

Quantitative Control of the Published Determinations of Glycyrrhizic Acid.

The Licorice Used for Control Experiments.

In order to carry through a critical work such as the present, it was necessary to investigate only one kind of licorice extract, so that the results obtained could be compared with one another. Although it might appear desirable to investigate the action and accuracy of the individual methods proposed, on different kinds of

licorice, say a very good one, a medium quality, and a very bad one, the work necessary to carry through this idea would spread beyond the limits of this task. Above all, time would not permit of exact and exhaustive treatment. With this thought in mind, after trying various kinds, I decided to use the Baracco brand for my control experiments. I obtained this from the firm of Caesar & Loretz. The method of our Pharmacopœia gave the following results:

Residue insoluble in water was 31 per cent.

11.4356 g. of licorice lost 1.8777 g. when dried at a 100° to constant weight, equivalent to 16.42 per cent. moisture.

The ash was 9.78 per cent. (4.324 g. licorice gave a residue of 0.4229 g.).

Characteristic of this licorice was its extraordinary content of copper. Every solution in water, even of quite small quantities, showed in the insoluble sediment a more or less large quantity of pure copper, sometimes as a powder and sometimes in large, long, flaked pieces. I have found pieces as long as 5 millimeters, and weighing as much as 0.062 grams.

In the present research, this was the only kind of licorice used. The controls covered over 100 individual glycyrrhizin estimations, and consumed more than half a year. In order not to be affected by changes in humidity, which would naturally cause changes in the moisture content of the licorice, I used a finely powdered extract, which had been dried for several days in a vacuum desiccator over sulphuric acid, and of whose moisture content I could be assured. An experiment showed that 5.0358 g. of dried licorice after drying to constant weight at a 100°, lost 0.2652 g. The dried licorice which I used for all this work therefore still contained 5.27 per cent. moisture. In order to obtain comparative results I naturally followed exactly the methods described. If, for any reason, this could not be done, I made particular note of it. If an author's directions were ambiguous, or if they seemed to me to be missing at some important point, I substituted, particularly when it was a question of volumes of liquids, amounts which seemed to me suitable for the case in point. On repeating particular experiments, I was naturally guided by the amounts added previously, in order to be able to compare the values obtained. I always conducted two determinations side by side by the same method. The experiments were repeated until I obtained average values which did not differ from one another by

more than 0.5 to 0.6 per cent. In spite of the greatest care, and keeping experimental conditions as nearly alike as possible, it was difficult to obtain values which agreed well. Many other investigators with glycyrrhizin have made the same observation. All weighings were made on a chemical balance to within one-half mg. Liquids were evaporated on the water bath. Drying to constant weight took place in a water oven which always showed 98° C. I also used this oven when the directions called specifically for 100°, being convinced that the difference of 2° was of less importance than the advantage of always having a uniform temperature.

SUMMARY OF THE PUBLISHED METHODS FOR GLYCYRRHIZIN DETERMINATION.

A. Extraction liquid: Water without the use of alcohol.
   Precipitation with sulphuric acid: (1) Rump, (2) Helfenberger, (3) Capin.
   Precipitation with hydrochloric: (4) French Pharmacopœia.

B. Extraction liquid: Water with addition of alcohol.
   Precipitation with sulphuric acid: (5) Diehl, (6) Kremel, (7) Py, (8) Parry, (9) Evans' Sons, Lesher & Webb, (10) Houseman, (11) Erikson, (12) Guignard.
   Precipitation with hydrochloric: (13) Gadais I, (14) Gadais II.
   Precipitation with absolute alcohol: (15) Trubeck.

C. Extraction liquid: Ammoniacal water without addition of alcohol.
   Precipitation with sulphuric acid: (16) Schröder, (17) Müntzer, (18) Morpurpo.
   Precipitation with hydrochloric: (19) Dutch Pharmacopœia.

D. Extraction liquid: Ammoniacal water with addition of alcohol.
   Precipitation with sulphuric acid: (20) Kinzey, (21) Anselmino-Gilg.
   Precipitation with hydrochloric: (22) Stoeder, (23) Telle, (24) Durier.

E. Extraction liquid: Alcohol-sulphuric acid.
   Precipitation with sulphuric acid: (25) Haffner, (26) Cederberg, (27) Schmidt (Haffner).

The control experiments which now follow are arranged in the order of this table.

1. Rump (1855).

"One part of licorice extract is dissolved in three parts of water. Half an ounce of the solution is diluted with one ounce of water, and one drachm of dilute sulphuric added. The washed and dried precipitate should amount to between five and seven grains."

Converted to our present system of weights, Rump would require that from a solution of 3.75 g. of licorice in 45 g. water, 0.3 to 0.42 g. glycyrrhizic acid should be separated by 3.75 g. dilute sulphuric acid. He therefore requires 8 to 11.2 per cent, a content which indeed corresponds approximately to present-day requirements. This method of Rump has, of course, only historical interest, as the first published glycyrrhizin estimation. I therefore did not attempt to check it up.

2. Helfenberger Annalen (1897).

"Five grams licorice extract are dissolved in 50 g. water, filtered, the filter washed with water, and 5 cc. dilute sulphuric acid added to the filtrate. The precipitate is collected on a small filter, washed well, dissolved in ammonia, filtered, the filtrate evaporated in a weighed dish, and the residue dried at 100° to constant weight."

A solution of 5 g. licorice in 50 g. water filters with great difficulty. I required in one case, eight hours to filter and wash that quantity until nearly colorless. The method in its description is so vague that one can obtain results which agree only when one completes the missing instructions. He says, "Filter, wash with water, and wash the precipitate thoroughly." These instructions, on account of their inexactness, must give large differences in the values obtained. To wash the insoluble residue, I used 50 cc. of water which, however, was not enough to obtain a completely colorless filtrate. To wash out the acid I used 30 cc. in small quantities. Dropping ammonia on the filter paper holding the acid, was not practical, as the liquid filters with great difficulty. As the instructions may also be interpreted I have dissolved the acid on the filter paper in warm ammonia, filtered, and washed the filter paper until colorless. From several experiments, I obtained between 6.9 per cent. and 7.2 per cent. yield, weighing 0.344, 0.348, 0.357, 0.360, 0.365 g. ammoniated glycyrrhizin from 5 g. licorice. From the method given in the introduction, I obtained as the loss from the 5 g. licorice 0.18-0.19 g. glycyrrhizic acid, corresponding to 3.6-3.8 per cent.

The high losses are caused by washing the precipitated acid with much water, and by the solubility of the acid in the supernatant liquid. I obtained 29 to 30 per cent. insoluble residue. Helfenberger's method does not attempt a purification of the precipitated acid. Since alcohol is not used to precipitate gums and other materials, the glycyrrhizic acid weighed is very impure.

Even in Helfenberger's "Annalen" of 1913, this method is used. It is surprising that it has not been improved in the course of years, since in latter years many practical proposals have been published.

3. Capin (1911).

"Two g. of licorice are dissolved in 20 cc. distilled water, the filtrate is transferred to an Erlenmeyer flask, 2 cc. sulphuric acid (66 per cent.) are added, and the vessel allowed to stand on ice with frequent shaking. After standing 24 hours, the liquid is poured on a smooth filter paper and the residue quickly washed by decantation with water at 0° to remove the last traces of sulphuric acid. The wash waters are passed through a second smooth filter, and the glycyrrhizic acid collected on this. Through the second filter is run 10-15 cc. distilled water containing 5 drops of ammonia to every 10 cc., and the liquid is received into the Erlenmeyer flask. The filter is washed with water, and the solution evaporated and weighed in a tared dish. The loss from 2 g. of licorice is reckoned as 0.11 and is added in."

This method uses the experience of a long research which I treated in detail, and aims to be an improvement of the method of the French Pharmacopœia. Although Capin's method may be regarded as an improvement, it contains a number of serious errors.

Two g. licorice are to be dissolved in 20 cc. of water, and the solution filtered. Capin uses no alcohol. This filtration requires a long time. From the filtrate, the glycyrrhizin is to be precipitated by sulphuric acid. Capin does not speak of washing the filter, although, of course, it should be obvious. If, however, one would wash until almost colorless, one would obtain a volume of more than 50 cc.. from which to precipitate glycyrrhizic acid (in one case I used 35 cc. wash water, and in three other cases none at all, since the method does not call for it). If one omits the washing, losses result from the material staying on the filter. But if one does wash the filter, the quantity of acid precipitated is diminished because of

the greater solubility in the increased quantity of water. The supernatant liquid is poured off from the acid, and the latter washed free from sulphuric acid by decantation with water at 0°. The quantity of water to be thus used is not stated. From 2 g. licorice, I weighed 0.140, 0.151, 0.156, 0.160 g. ammonium glycyrrhizinate, that is 7-8 per cent. This amount would be increased to 12.7-13.5 per cent. by the improvements mentioned below.

These values are too low, more particularly because of the losses from the solution remaining on the filter. I found the loss from 4 g. of licorice to be 0.051 and 0.061 g. of glycyrrhizic acid, *i. e.*, 1.25-1.53 per cent. On the filter there remained 32 per cent. of insoluble matter. It can be seen from the above that this method has been badly worked out, and the necessary directions for obtaining accurate results are missing. This method can therefore give only unsatisfactory results. No purification is prescribed, and Capin does not use alcohol in spite of the great advantages obtainable thereby. The ammonium salt weighed is therefore very impure. Capin makes the very interesting experiment of decreasing the solubility error by adding a factor, good for every case, to the value obtained. In the introduction I have already pointed out that Capin obtained this solubility factor by shaking up an excess of glycyrrhizic acid with water and estimating the soluble part at 15° and 0°. He calculates the factor for 20 cc. of liquid precipitated and so obtained the number 0.110 to be added to the value found for ammoniated glycyrrhizin. This improvement is wholly undemonstrated and lacks any real basis. The following objection applies to it: The solutions used in glycyrrhizin determinations are never saturated, but are always quite weak. This is particularly the case with those solutions which are to be corrected for losses through washing.

[TRANSLATOR'S NOTE.—Here follows a half page more of further objections to Capin's method. (P. A. H.)]

4. French Pharmacopœia (1908).

"Two g. licorice are taken up in aqueous solution, filtered, made to 100 cc. and 30 drops of hydrochloric acid are added. After standing 24 hours, the liquid is poured through a filter, the residue and filter washed three times with 8 cc. portions of water, and then 10-15 cc. water, containing 5 drops of ammonia per 10 cc. is poured through this filter. The filter is washed with distilled water, and the solution of

ammoniated glycyrrhizin is evaporated to dryness on the water bath, and weighed. A weight of at least 0.2 g. is required."

This Pharmacopœia method does not state in how much water the licorice is to be dissolved. I always used 30 cc. and washed the insoluble residue until I had 100 cc. filtrate. The filtration took a long time. For the precipitation, 30 drops of official hydrochloric acid were used (Sp. Gr. 1.171, 22° Be.), which method I adopted. The filtration of the precipitated acid takes a very long time if a smooth filter is used. Therefore in the following experiments I always used a fluted filter. Three 8 cc. portions of water are not sufficient to wash the glycyrrhizin precipitate until colorless. There is, therefore, the possibility, that water-soluble materials which should be washed out, are later weighed as ammoniated glycyrrhizin. It is quite incomprehensible why the French Pharmacopœia specifies a solution of the glycyrrhizin salt in 100 cc., and precipitates the acid from this large volume of water. Twenty cc. of liquid would be quite sufficient. The use of such a large excess of water results in very appreciable losses. The precipitation takes place with hydrochloric acid, but the amount of acid prescribed is much too small, so that not all of the glycyrrhizin is precipitated, an observation which Capin himself made. If after adding the hydrochloric acid according to directions, the mixture is allowed to stand 24 hours and the glycyrrhizin filtered off, the filtrate shows a further precipitate on standing when additional hydrochloric or sulphuric acid is added.

[TRANSLATOR'S NOTE.—Other objections to this method are mentioned, including the fact that alcohol is not used. (P. A. H.)]

The values which I have found for the losses involved, prove sufficiently that the method of the new French Pharmacopœia is entirely useless. It is really quite remarkable that even in 1908 such a poor method could be adopted when a whole series of publications were available which would have given practical results.

5. *Diehl (1883).*

"Ten g. licorice are digested, until disintegrated, with 10 cc. distilled water in a flask. After cooling, 200 cc. of alcohol are added, and allowed to stand several hours with frequent shaking. The liquid is then filtered through a double filter and the residue washed with a mixture of alcohol and water (2:1) until the filtrate is colorless. The alcoholic filtrate is evaporated to a syrup, dissolved in

water, and sulphuric acid added as long as a precipitate forms. The glycyrrhizin is washed with water, dried in the air and dissolved in strong alcohol. The alcoholic solution of the acid is filtered, the filter paper washed with alcohol, and the solution evaporated to dryness. The residue is dissolved in ammonia, and evaporated, dried, and weighed in a tared porcelain dish."

Diehl precipitates gummy and mucous substances with a large quantity of alcohol. The filtered and evaporated alcoholic extract is dissolved in water. The quantity is not stated, and further, the amount of sulphuric acid to be used for precipitation is not given. I also fail to find any statement as to how long the precipitate is to stand, and how much water is to be used for washing. In order not to obtain different results on account of these missing instructions, I supplied those which seemed to me to be suitable. I dissolved the evaporated extract in 60 cc. of water, precipitated with 5 cc. dilute sulphuric acid, and washed afterwards with 50 cc. water. Diehl now attempts a purification of the precipitated acid by re-dissolving in strong alcohol, previously drying the acid in air. If one takes freshly precipitated glycyrrhizic acid which is not quite dry, and treats it on a filter paper with absolute alcohol, one can wash the filter quite white, without any trouble, particularly if one warms the alcohol a little. If, however, one makes the precipitated acid quite air dry, perhaps even in a desiccator, it is then found that a part of the acid has become quite insoluble in alcohol. Since one can scarcely assume that glycyrrhizic acid, through simply standing a few hours in the air, or in a desiccator, would be decomposed, and since, further glycyrrhizic acid is soluble in hot absolute alcohol, one must regard the residue remaining on the filter as an impurity. An explanation for the different behavior of the moist and dry acid toward alcohol, is difficult to find unless one considers the possibility that the very small amount of water remaining on the filter in the first case dilutes the absolute alcohol, and so dissolves the glycyrrhizin. Such an influence, however, could only be effective for a few moments, since the absolute alcohol at once penetrates the filter. I must accept as the only possible explanation, the formation of a colloidal solution. In any case, I am of the opinion that this residue, which is insoluble in alcohol and easily soluble in ammonia represents impurities in the acid. Since such a purification is easy to carry out, its use in the quantitative determination is certainly to be recommended.

The insoluble residue on the filter, I dissolved in ammonia and evaporated in a weighed crucible. The weight varied between 0.09 to 0.11 g. There is therefore 0.9 to 1.1 per cent. weighed as ammoniated glycyrrhizin, which only consist of impurity in the acid. The ammoniated glycyrrhizin, obtained by Diehl's method is of a much lighter color than that from other methods. The difference is very noticeable. It is remarkable in this determination, that Diehl does not simply weigh the alcoholic solution of glycyrrhizic acid which he evaporates to dryness. Instead of that, he dissolves the dry residue again in ammonia, transfers to a tared dish, and weighs after drying again. This unnecessary, roundabout way results in much loss of time, and only renders errors possible. I obtained from 10 g. licorice 8.24-8.44 per cent. As losses, I obtained 1.91-2.11 per cent. The insoluble matter was 39-40 per cent. of the licorice taken.

The method of Diehl, in the form given, cannot be used on account of such vagueness. If, however, the missing instructions are intelligently completed, and one omits the useless conversion of the dried acid to the ammonium salt, one obtains good results, and a precipitated acid of a high degree of purity.

6. Kremel (1899).

"For the estimation of glycyrrhizin, 5 g. of roughly-broken licorice extract are dissolved in 50 cc. water, and allowed to stand several hours with frequent stirring. After disintegration, 50 cc. of 90 per cent. alcohol are added, stirred, the mixture allowed to settle, and filtered through a small fluted filter. The contents of the filter are thoroughly washed with 40 per cent. alcohol. The alcohol is evaporated from the filtrate on the water bath. After cooling, sulphuric acid is added to precipitate the glycyrrhizin. This is collected on a small filter, well washed with distilled water, and finally brought into solution by dropping ammonia on the filter. The ammoniated glycyrrhizin is collected in a dish, evaporated to dryness on a water bath, dried at 100° and weighed."

Kremel's method is inexact in some details, so that comparative values cannot be directly obtained from it. It is not stated how much alcohol is used to wash the insoluble matter. I found 50 cc. yielded a nearly colorless filtrate.

[TRANSLATOR'S NOTE.—Other sources of error due to vagueness are mentioned, including failure to specify quantity of sulphuric acid and of water used for washing the precipitate. (P. A. H.)]

The method discussed above which was published in 1889 has become the basis for a large number of methods published later. Although certain changes have been introduced in these later methods, the principle has remained the same. After intelligent completion of missing or faulty directions, the method gives practical results.

7. Py (1897).

"Two g. licorice are dissolved in about 30 cc. water on the water bath. After cooling, alcohol is added until a strength of 75 per cent. alcohol is attained. After standing 12 hours, the mixture is poured through a fluted filter, and the filter and residue washed with 75 per cent. alcohol. The alcohol is evaporated, the residue dried at 100°, and weighed. It is then dissolved again in lukewarm water, and treated with dilute sulphuric acid (1:9). The precipitate is collected on the filter, and washed, first with water acidified with sulphuric acid, and then with distilled water, and finally dissolved from the filter with saturated ammonia-water. The filter is washed with ammonia until colorless. The ammoniacal solution is evaporated, dried at 100°, and weighed."

This method does not give detailed instructions, and further makes rather many inexact statements. Otherwise it does not differ from the others.

[TRANSLATOR'S NOTE.—The author (Linz) also objects to evaporating the alcoholic solution to dryness, also to the fact that Py does not state quantities for dissolving the dry alcoholic extract in water, for sulphuric acid used in precipitation, and for acidified water used in washing. In control experiments, Linz obtained 7.6-8.15 per cent. ammoniated glycyrrhizin with losses estimated at 2.22-2.75 per cent. The insoluble matter he determined as 47 per cent. (P. A. H.)]

This glycyrrhizin determination gives, therefore, the usual values if one intelligently completes the many inexact instructions. If one does not do this, one cannot obtain comparative results. The method in its original form cannot, therefore, be used.

8. Parry (1910).

"2.5 g. licorice are covered with 15 cc. hot water, and warmed on the water bath until dissolved. After cooling, 25 cc. 80 per cent. alcohol are added slowly with stirring and then 50 cc. 95 per cent.

alcohol. The liquid is allowed to stand half an hour, then filtered, and washed with 80 per cent. (by volume) alcohol until colorless. Filtrate and washings are evaporated to a syrup to remove the alcohol. The residue is transferred to a flask and made up to 30 cc. with water. Three cc. of dilute sulphuric acid (10 cc. of H_2SO_4 plus 300 cc. water) are added slowly with stirring. After allowing to stand over night at 12°-15°, the liquid is decanted, and the precipitate washed four times with ice water, and dissolved in alcohol. To neutralize free sulphuric acid 2 drops of ammonia are added, and the solution evaporated on water bath to constant weight in a tared dish."

The method of Parry gives the usual picture of a glycyrrhizin determination. With a few changes this method has been adopted by Evans' Sons, Lesher & Webb, and by Houseman. The gums are precipitated with much alcohol, etc. The proportion, 2.5 g. of licorice to 15 cc. water, is in my opinion, the strongest solution which can be used without fear of loss. The addition of alcohol to give a mixture of 80 per cent. strength is presumably the strongest alcoholic solution which may be used. The good results obtained show that, by the experimental conditions given, losses do not result. The alcoholic solution after evaporation is taken up to 30 cc. In my opinion this volume is correctly chosen according to experience. The requirement to stand overnight at 12°-15° C. is probably not always called for. The supernatant liquid is to be poured off, and the acid is to be treated by washing and pouring off four times with ice water. I only succeeded twice in getting the glycyrrhizic acid to stick to the bottom so that it could be washed without loss. In such a case one must take a more roundabout way, collecting the acid on the filter and then dissolving it in hot alcohol. By this treatment losses are not excluded. Unfortunately Parry gives no quantities for washing with ice water, but it is highly necessary to prescribe exact quantities. The values received in checking the method are good. I obtained from 2.5 g. licorice, 0.230, 0.234, 0.239, 0.249, 0.249 g. glycyrrhizic acid, *i. e.*, 9.44-9.96 per cent. The losses on 5 g. licorice I determined in two experiments to be 0.0284-0.0314 g. glycyrrhizin, *i. e.*, 1.1-1.3 per cent. I found about 49.5 per cent. insoluble matter. In summarizing, I would state that the Parry method gives usable results, although a purification of the acid is not attempted.

9. Evans' Sons, Lesher & Webb (1910).

"2.5 g. of finely powdered material are weighed into a little beaker, 15 cc. water added, and warmed on the water bath to dissolve. After cooling, 23 cc. technical alcohol mixed with 2 cc. water, are added with stirring, and then 50 cc. alcohol. After standing for half an hour, the liquid is filtered into an evaporating dish and the precipitate is washed with a mixture of 50 cc. of technical alcohol with 4 cc. water. The filtrate and washings are evaporated to a syrup on the water bath, transferred to a thin-walled glass cylinder with 30 cc. water, cooled in melting ice and mixed with 3 cc. sulphuric acid (1-30). The contents of the cylinder are brought to freezing in an ice-salt mixture, and the glycyrrhizin is obtained as a solid mass on the bottom of the cylinder by allowing to thaw slowly. It is washed by decantation with 50 cc. water at 0°, and as much of the liquid decanted as possible. Two cc. ammonia water are then added, and the precipitate transferred to a weighed crucible with absolute alcohol, evaporated and dried at 100° to constant weight."

This method is founded on that of Parry. The numbers, quantities and strength of alcohol agree exactly. The only new thing is the attempt to use the fact that glycyrrhizic acid is more difficultly soluble in water at 0° than in water at room temperature. Against the practicability of this idea, which is good in itself, I have objections which I will hereafter explain. This method was only available to me in a translation (*Jahresbericht der Pharmazie,* 1910, p. 239). As I did not understand the expression "Technical alcohol" in the translation, I requested information from the Editor of the "Chemist and Druggist." I then learned that "technical alcohol" (Industrial methylated spirits) has the same significance as our "vergällten spiritus." This spirit is denatured with wood naphtha, which corresponds to our pyridin bases, in the proportion of 19:1. I considered that I might dispense with the use of denatured alcohol in my check experiments since its use is only explainable by the fact that pure alcohol is so extremely expensive in England. The mixtures describing this method, as regards strength of alcohol, are exactly the same as Parry's, so that my remarks on the latter apply. In my opinion, one-half hour's standing is not enough to precipitate all the starch and gums. At any rate, in a control experiment it was found that after standing and filtering according to directions there formed after a few hours a further light precipitate, which could only consist

of gums not previously precipitated. These gums could possibly have been weighed finally as glycyrrhizic acid. The filtrate is then to be evaporated to a syrup, and transferred with 30 cc. water to a thin-walled glass cylinder. I used a wide test tube for this purpose.

[TRANSLATOR'S NOTE.—Linz goes on to show that the proposal of Evans to obtain the glycyrrhizin sticking to the bottom of the vessel by freezing and subsequent thawing is a good idea, but unfortunately does not work out in practice as described. Linz tried it six times unsuccessfully. (P. A. H.)]

(*To be Continued.*)

PLANT COLORS

By DR. HENRY KRAEMER, Mt. Clemens, Mich.

The nature of plant color has been the subject of some investigation and considerable speculation. There is no objection to constructing theories concerning the origin, nature and functions of plant colors, providing we recognize that they are apt to be, with our meager knowledge of plant color substances, mere speculations, and it is doubtful if any of our theories will stand the test of time as new investigations are made. There are probably a few facts that we recognize, and some of these may be briefly stated as follows:

1. The name anthocyanin as first given by Marquardt may be used to designate all the plant colors, other than the green and yellow which are plastid colors. The anthocyanin colors usually occur in the cell sap and may be present in flowers fruits, roots and leaves of higher plants, or even in the lower plants.

2. In the marine algæ the anthocyanin colors seem to be contained in plastids and are usually not liberated and distributed free in the cell until the death of the filament. In the higher plants the anthocyanin colors are usually present in the vacuoles of the cell and are usually of either a blue or red color, but many intervening shades of red and blue are to be seen.

3. The blue anthocyanin are variously distinguished, some being quite permanent as in the flowers of Delphinum, Viola and Malva, even on the death of the cell or drying of the plant, whereas in other plants they are decomposed, changing to a fawn or brown color, as in the flowers of Pawlonia, Bellis, etc.

4. The blue anythocyanin colors may separate under certain conditions as when there are marked changes in temperature or other disturbances in the cell in the form of either spherical globules, which may be relatively numerous as in the petals of Catalpa or in larger globules as in the petals of Cinearia, Delphinium and blue hydrangeas, or may show a spherite structure or separate in the form of long rods as in the leaves of red cabbage.

5. The red anthocyanin colors are of two kinds:

a. Those which change to a blue or purplish red as in the rose, mertensia, tiger lily, tulip, cineraria, dogwood, red hydrangea, and red cabbage.

b. Second class includes those red anthocyanins which do not change in color as in red apples and in nearly all of the red fruits.

6. Anthocyanin colors may also occur in the same cells which contain either chloroplastids or chromoplastids. As examples in which both chloroplastids and anthyocyanins occur in the same cell may be mentioned the leaves of wild carrot, the beet, and purple beech. Chromoplastids and anthocyanin colors are frequently to be found in flowers as the nasturtium and tiger lily.

7. Anthocyanin colors while found in the stems and leaves, and also in thorns as in roses are usually more pronounced or more strongly developed in those organs at the extremity of the plant or at the tips or shoots as in the purple beech and in flowers generally.

8. Plant color substances from their solubility may be grouped into two classes:

a. Those while like the plastid color substances are insoluble in water and soluble in immiscible solvents as petroleum benzine, toluol, ether, etc.

b. Those which are soluble in water or at least in hydro-alcoholic solutions, but insoluble in the immiscible solvents.

9. The investigations of plant color substances show that they may be brought into probably three groups:

a. Colorless, or leuco-compounds, which upon oxidation form distinct color substances as in the lichens.

b. Glucosides, which on the action of ferments yield color substances as those forming the yellow pigment, quercetin.

c. Substances which possess a basic radical or chromophore, and which manifest distinctive colors depending upon the arrangement of certain groups and side chains. There is a disposition by some authors to consider that the shades of color are due to an enzymic action on the chromatin. It is not easy to refute this latter claim as enzymes are always present in the plant cell, and it is not always easy to dissociate the action of the enzymes from that of other substances which are capable of producing equal changes in the color of a pigment. That there are very many substances capable of producing color changes in plant pigments is well known, but unfortunately these changes are not due in the plant cell to the replacement of the hydrogen ion with some basic radical. A microscopical study of plant organs containing anthocyanin colors usually show in the different cells varying reactions which, while they might be ascribed as being due to enzymes, are more likely to be the result of the interaction with other substances.

SOME EXPERIMENTS ON THE MODIFICATION OF COLOR IN PLANTS.

By Dr. Henry Kraemer, Mt. Clemens, Mich.

The study of color in plants may be pursued in several directions: 1. They may be biological or functional. 2. They may be chemical or constitutional. 3. Or they may be physiological or cellular. Studies involving any experiments with the view of modifying color in plants are fundamental studies connected with the physiology of the plant cell.

Probably the most fundamental studies are those which are of a chemical nature in which the constitution of color compounds is

demonstrated. On the other hand, such studies are quite difficult, and usually will involve considerable expense, as large quantities of material are necessary in order to obtain a given constituent. It is my object in this paper to report on some experiments which I conducted nearly ten years ago with a view of modifying color in flowers. These studies have not been previously reported upon, because the results at that time did not seem to be sufficiently strongly marked, and unless the paper was illustrated with colored plates, no adequate idea of these changes could be seen. Fortunately all of the work which I did at that time is conserved either with colored photographs or with drawings in which the shades of color were quite accurate. Upon resuming my work in the study of color in flowers I have become impressed with the fact that this earlier work was really more valuable than I thought at the time.

Studies of changes of the color in flowers, the plant being in a fixed environment is essentially a physiological study of the plant soil.

Upon the sea coast the flowers of the *Hydrangea Otaksa* invariably become blue in the second year even though the flowers in the plants were pink or a strong reddish color. This is usually attributed to the salt air, the fine spray of sodium chloride having an influence on the color change. The older, weakly woody plants of *Hydrangea Otaksa* almost invariably have a tendency to produce blue flowers, although in many environments the plants will run into foliage and not produce any flowers at all. It is a very common belief that the flowers of hydrangea may be changed by the introduction of chemicals into the soil. In fact, very many gardeners who are anxious to have blue flowering hydrangea plants at Easter time, invariably add a piece of alum about the size of a walnut to the soil of the pots during the summer. The study of the pigment cells of any portion of the plant shows that the change of color would be produced by a great variety or reagents. It is quite well known that the substances of the soil may be changed by the introduction of chemicals or other soils. These produce changes in the plant cell. The carbohydrates for instance in a green algæ may be changed into reserve starch by adding calcium nitrate to the water surrounding them. In the same way a reserve starch will be duplicated in the cells of foliage leaves when they are attacked by certain fungi.

The colored areas of the plant are generally located at the terminal portions and are usually located in the tissues in the periphery of these organs. It is quite likely and seems very reasonable that if the proper chemicals were supplied the plant in an unaltered form or if they could be supplied in such a form that they would be altered by the cell distinct color changes would ensue. In other words the same change would be attained as we find on treating the pigment cells upon a slide with reagents or substances which are usually present in the soil and water. It is quite possible that studies on the algæ would yield some striking and variable results in this particular. The great difficulty would be in noting this change in color, which, however, could be followed by the device which I have made for use in the study of color in higher plants. Again, before taking up flower color substances this work might be developed in the study of color in root-like organs, in the raddish.

In my own experiments I think the mistake that was made was in not studying more extensively the distribution of colors in flowers than I did. Subsequent studies show that the pigment is distributed in four ways in the flower: 1. The pigments are usually in epidermal cells as in the rose and pansy. 2. The pigment may occur in subepidermal cells in addition as in wild hyacinth. 3. It may occur in the mesophyl layers in addition as in Mertensia. 4. It may occur in the conducting tissues surrounding the mestome strands in the flower as in blue hyacinth. From this study of the distribution of flower color substances it would seem that if the study was made of those plants in which the pigment in the flowers was in the immediate proximity of the fibro-vascular bundles that the chemical supplied the plant through the soil might be more or less unaltered and produce communication in the pigment cells.

Of course, there are a number of other features that are fundamentally important and that should be ascertained only at the time of formation of flower coloring process. It would appear that these are usually formed some time after the organs of the flower have been formed. However, in the foliage of very many plants that produce flowers there are indications that the pigment is formed in the early stages of organs in which photosynthesis takes place, as in the rose. In fact, the pigment in the foliage of the rose as well as in the prickels closely correspond to the pigment of the flowers.

STUDIES IN EXTRACTION.

By JAMES F. COUCH.

I. THE RATE OF EXTRACTION OF PHYTOLACCA DECANDRA.

In a general survey of the theory of percolation [1] I have pointed out the desirability of more data on the rates of extraction of various drugs to fill in certain gaps in our knowledge of percolation. The rate of extraction may be determined in several ways: In this paper and in two which are in course of preparation, three methods have been employed which differ only in extensiveness. Data already published on the rates of extraction may be found in the published works of Lloyd, Squibb, McIntyre and Robbins, reference to which may be found in above quoted survey.

The previous work on this subject, however, was carried out at the time when the standard for fluidextracts was a grain per minim instead of a gram per millilitre as at present, and the modern fluidextract is but 95.14 per cent. of the strength of that of forty years ago. As the earlier work was conducted with reference to the former standard it is highly desirable that it should be reviewed with respect to the present standard for the sake of exactness and completeness. In addition, the earlier work was conducted particularly so solve questions of economy of menstruum, of time, or in attempts to avoid evaporation of weak percolates.

The following account presents the results of an inquiry into the factors which govern the rate of extraction of phytolacca, the generalizations which underlie it, and the conditions which obtain. The theory of the process has already been discussed.[2]

It was found that the extraction of phytolacca proceeds in a regular manner, but with diminishing velocity, so that the last portions of extractive require a considerable volume of menstruum for their removal. This is in conformity with the published results of all previous investigators which bear at all on the subject. There appears to be a point where the cellulose of the drug exerts an attraction for the extractive equal to that of the mestruum for the extractive. At this point equilibrium will be established and the

[1] This *Journal*, Vol. 92, Nos. 11 and 12 (1920).
[2] This *Journal*, Vol. 92, p. 788, *seq.* (1920).

velocity of the extraction will become zero. The extraction of phytolacca is extremely rapid at the beginning of the process, and when a volume of percolate thrice the amount of the fluidextract equivalent to the weight of the drug had been collected, 97 per cent. of the total extracted matter had been dissolved out of the drug. In other words, the percolation of one gram with three millilitres of menstruum removed 97 per cent. of the total extract obtained.

In accordance with this assumption that the attraction of the marc is one of the factors which govern the rate of extraction of a drug a number of mathematical formulas were applied for the purpose of calculating a constant distribution ratio between menstruum and marc. The results in all cases showed a progressive variation, either a numerical increase or a decrease and no constant was obtained. (Fig. I.) Other factors intervene, and these are probably the same as those which affect the velocity constant discussed below.

The results obtained in the actual extraction are plotted in Fig. II, where the ordinates represent grams per 100 ml. (additive), and the abscissæ gallons of percolate. This curve shows the regularity of the extraction, the rapid initial extraction, and the retardation which sets in later in the process. It may, with profit be compared with the plotted results of an extraction of cimicifuga reported by Lloyd,[3] which shows the same general characters. It will be noted that the cimicifuga was extracted much more rapidly than in phytolacca. Lloyd used 7680 grains of drug and 97 per cent. of the total extract was contained in the first 21 floz. of percolate. In order to duplicate that rate the present extraction would have to show 97 per cent. in the first six and one-half gallons, or about twice the true rate of extraction. The cimicifuga yielded about 5 per cent. and the phytolacca 32.75 per cent. of extract; consequently the difference in rate of extraction was not due to the amount of soluble matter in the drugs, but rather to a difference in solubility. It is thus apparent that phytolacca is more easily extracted than cimicifuga.

In attempting to apply a mathematical treatment to the rate of extraction it was decided that, since we have no quantitative knowledge of the various constituents of phytolacca, the quantity of extract should be dealt with as a unit. A number of formulas were applied, but all of them gave a series of results which exhibited the

[3] This *Journal*, 59/434 (1878). The results are plotted in this *Journal*, Vol. 92, p. 857 (1920).

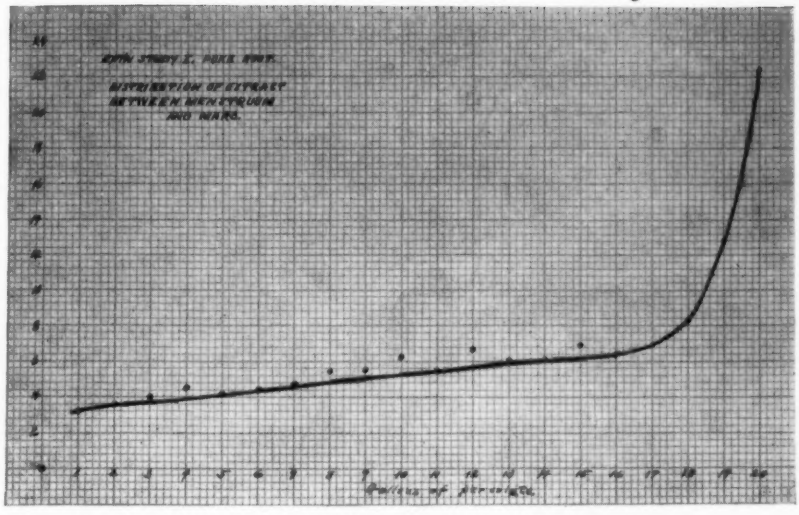


FIGURE 1.

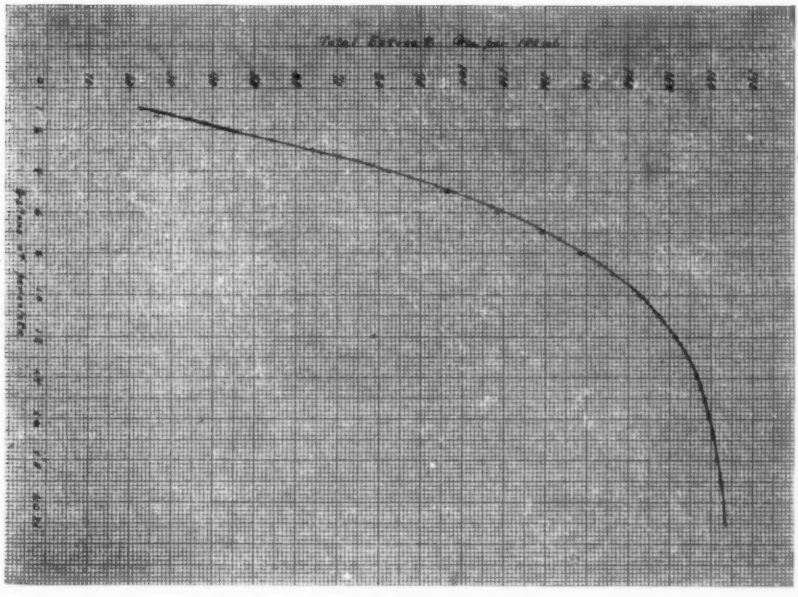


FIGURE 2.

same numerical increases or decreases observed in the attempt to calculate a distribution ratio. The factors applied in these formulas were functions of the concentration of extracted matter, undissolved extractive (this included that in the marc, that dissolved in the absorbed menstruum, and that dissolved in the percolate) and time. The lack of constancy in the results indicates that there are other factors which influence the rate of extraction, and we may here consider two: (1) Variation in the composition of the extract;[4] the more soluble matters are extracted first, leaving the more refractory substances to the less saturated portions of the menstruum; and (2) variation in the alcoholic strength of the menstruum,[5] with a consequent change in its solvent powers. The observed difference in alcoholic strength between the first and the twentieth gallons of percolate in this extraction was over 7 per cent. The first few gallons were diluted by the natural moisture of the poke root, which amounted to three or four pints, a quantity capable of seriously altering the solvent power of the menstruum. The fact that the alcoholic strength of the menstruum increases would lead to an assumption that the solvent powers of the menstruum increase as percolation proceeds and it is possible that, as the drug becomes more difficult to extract, the menstruum becomes more able to dissolve the extractive, but not proportionally. The two factors will thus tend to neutralize one another. With our present knowledge, however, it does not seem possible to characterize the rate of extraction of any drug by a factor which will represent conditions at any point in a percolation.

EXPERIMENTAL.

A quantity of phytolacca was purchased on the open market, identified, and ground to a coarse powder; 19,876 Gm. of this drug were percolated according to the directions of the U. S. P. 8. The drug was mixed with five gallons of diluted alcohol in a mechanical mixer, and the whole was packed firmly in a galvanized iron percolator of about twenty-five gallons capacity. This particular weight of drug was chosen so that the experiment might furnish somewhat more than five gallons of fluidextract of official strength.

The percolator was set in place, enough menstruum was added to displace the air and leave a stratum above the drug. The appara-

[4] Cf. Squibb, this *Journal*, 38/109 (1866); 39/402 (1867); 40/1 (1868).
[5] Cf. Lloyd, Proc. A. Ph. A., 1881/408; 1882/508.

tus was then tightly closed and was allowed to macerate exactly 48 hours when percolation was commenced. The flow of percolate was so adjusted,[6] that one gallon of percolate was obtained in about one hour and one-half. The percolation was discontinued at 5.30 P. M., and was recommenced at 8 A. M. the following day. The procedure followed in collecting the samples was this: Each gallon of percolate was collected separately in a clean bottle connected by a rubber tube with the percolator to avoid contact with the air. The whole gallon was thoroughly mixed and a portion was then taken for analysis.

During the process the temperature of the percolator varied from 23° to 26° C. Fresh menstruum was added continually to replace that percolated out.

The specific gravity of the samples was determined on a Westphall balance standardized against water at 0° C. Alcohol was determined in a few samples by distillation of 50 ml. samples, dilution of the distillate to 100 ml. and determination of the alcoholic content from the specific gravity at 15.6° C.

The extract was determined by the following procedure: 25 ml. of the percolate were pipetted off into a weighed evaporating dish; the pipette was rinsed with 10 ml. of distilled water and the rinsings were added to the sample. This was then evaporated to constant weight on a water bath and was then heated to nearly constant weight in an oven at 105° C. The weight of extract so obtained multiplied by four gave the extract per 100 ml. Of course, volatile oils were driven off and lost. Check determinations of this method showed it to be accurate within 0.5 per cent.

The data obtained by the analyses and some of the calculations are recorded in Table I.

TABLE I, PART I.

Date.	*Time.*	*Sample.*	*S.G.*	*Extract. Per 100 ml. (E.)*	*Per Gallon.*	*Alcohol by Vol.*
June 17.	9.25 A. M.	1	1.0448	22.40 Gm.	848. Gm.	31.65%
" "	11.15 "	2	1.0415	21.60	817.7	
" "	1.10 P. M.	3	1.0355	20.12	761.6	
" "	2.45 "	4	1.0261	18.38	695.8	32.5
" "	3.55 "	5	1.0157	14.04	531.5	

[6] Cf. Discussion, this *Journal*, Vol. 92, p. 854 (1920).

Date.	Time.	Sample.	S.G.	Extract. Per 100 ml. (E.)	Extract. Per Gallon.	Alcohol by Vol.
June 17,	4.55 "	6	1.0023	12.16	460.3	
" "	5.40 "	7	0.9946	10.58	400.5	33.7
" 18.	8.25 A. M.	8	0.9861	9.56	361.9	
" "	9.50 "	9	0.9800	7.42	280.9	
" "	10.55 "	10	0.9689	6.54	236.4	37.5
" "	11.55 "	11	0.9648	4.68	177.2	
" "	1.15 P. M.	12	0.9608	4.12	156.	
" "	2.15 "	13	0.9582	2.82	106.8	
" "	3.20 "	14	0.9558	2.20	83.3	38.3
" "	4.10 "	15	0.9546	1.84	69.7	
" "	5.00 "	16	0.9528	1.30	49.2	
" 19.	8.20 A. M.	17	0.9514	1.04	39.4	38.16
" "	9.15 "	18	0.9474	0.88	33.3	
" "	10.15 "	19	0.9465	0.82	31.04	
" "	11.25 "	20	0.9460	0.68	25.7	38.68
" 21.	Noon.	21	0.9489	0.60		

TABLE I, PART 2.

Total Extracted Per 100 ml.	Extract Left in Drug (500 Gm.) (D.)	E/D.	1/t.log E/D.	% Unextracted.	% of Residue Extracted.
22.40 Gm.	141.38 Gm.	0.1621	0.1239	90.38%	90.38%
44.00	119.38	0.1803	0.1526	80.19	88.73
64.12	99.66	0.2018	0.1653	69.87	87.13
82.50	81.28	0.2261	0.1745	59.57	85.26
96.54	67.24	0.2088	0.1780	50.87	85.41
108.70	55.08	0.2207	0.1816	43.01	84.53
119.28	44.50	0.2377	0.1861	35.69	82.96
128.84	34.94	0.2736	0.1931	28.74	80.54
136.26	27.52	0.2759	0.1982	23.10	80.38
142.80	20.98	0.3117	0.2054	17.93	77.63
147.48	16.30	0.2871	0.2097	14.12	78.72
151.60	12.18	0.3382	0.2166	8.97	63.56
154.42	9.36	0.3012	0.2202	8.26	92.17
156.62	7.16	0.3072	0.2235	6.36	76.99
158.46	5.32	0.3466	0.2284	4.61	75.88
159.76	4.02	0.3233	0.2317	3.60	74.69
160.80	2.98	0.3489	0.2357	2.67	74.35
161.68	2.10	0.4190	0.2480	1.89	70.65
162.50	1.28	0.6406	0.2659	1.15	61.10
163.18	0.60	1.1231	0.2804	0.54	46.79
163.78					

On June 21st, after the drug had macerated for 48 hours, the twenty-first sample was collected. The analysis of this showed the drug to be pharmaceutically exhausted.

The finished fluidextract yielded the following data: Alcohol, 37 per cent.; extract, 32.54 Gm. per 100 ml.; S. G. 1.0371.

SUMMARY.

1. The extraction of the root of Phytolacca decandra proceeds regularly with diminishing velocity.

2. The rate of extraction is proportional to the total extract, inversely proportional to the residual extractive, the time, and an unknown factor or combination of factors. On account of these unknown factors a number characteristic of the extractibility of the drug cannot be assigned it.

3. It is probable that the unknown factors depend upon a change in the composition of the extract and a rise in the alcoholic content of the percolate.

4. The first fifteen gallons of percolate contained 97 per cent. of the total matter extracted.

5. It is shown that the alcoholic content of the percolate increases as the percolation proceeds. This has not hitherto been demonstrated.

THE ASSAY OF ACONITE.

By Dr. A. R. L. Dohme,

Chairman, Committee on Aconite of Scientific Section of American Drug Manufacturers' Association.

The work covered by this paper represents what has been done during the past three years by the Scientific Section of the American Drug Manufacturers' Association, who have felt that its results should be made known to the medical and pharmaceutical professions generally.

The primary problem was to attempt to decide whether the chemical assay of aconite and its preparations had any real value, and the resultant problem was to determine if the physiological assay was accurate and trustworthy. The present official assay process U. S. P. IX Revision is a chemical one with an alternative physiological assay, but the chemical assay is the standard. In the VIII Revision there was only a chemical assay as the official process. In

both cases the end product was represented by ether soluble alkaloids. We have shown that the ether soluble alkaloids are not all aconitine, but represent a more or less variable proportion of aconitine and its products of hydrolysis benzoyl-aconine and aconine. This variability alone makes the assay process of little value as an absolute standard of therapeutic efficiency and as well makes its relative or comparative value more or less of an uncertain quantity.

In order to determine definitely if the three alkaloids which constitute the ether soluble alkaloids—aconitine, benzoyl-aconine and aconine could be separated from one another by chemical means a supply of pure aconitine was procured and hydrolized into benzoyl-aconine and some of the latter hydrolized further into aconine. After thus coverting a number of grammes in this way and obtaining a quantity of each of benzoyl-aconine and aconine in pure condition, attempts were made to determine if varying solubility in all available solvents or precipitation by all known precipitants might give a method of separating them when contained in a mixture. The result, however, was that no method was discovered by which they could be quantitatively separated, as they showed similar solubilities and precipitation by precipitants. It was, therefore, decided that a chemical separation quantitatively was not feasible and that, therefore, the so-called chemical method of assay was not possible, provided our aim was to get as the end-product of our assay only aconitine.

It was also determined by animal experiments that benzoyl-aconine and aconine do not possess the therapeutic properties of aconitine and their lethal dose was quite far removed from that of aconitine.

Hence the final conclusion reached was that the present chemical assay of aconite for ether soluble alkaloids was misleading and untrustworthy and had better be abandoned.

The next part of our problem was to see if a physiological assay could be developed which would be of some real value in determining approximately correctly the therapeutic efficiency of aconite and its preparations. This, of course, at once opens up the question as to the correctness of a method of assay which has as its criterion and basis the lethal dose or the amount that will kill a definite weight of animal per gram. Or in simple form is lethal power a basis for therapeutic efficiency, and is one drug that will kill 300 gm. of guinea pig in a dose of one milligram twice as efficient therapeutically upon

human beings as one that will kill 300 gm. of guinea pig in a dose of two milligrams. On this question pharmacologists and physiologists are apt to divide and differ. As lethal dose is the basis used in physiological assay methods, it is probably the only, and hence the best basis available for determining relative therapeutic efficiency of the drug.

Beginning with the pure aconitine crystals we used for making our hydrolysis products for above experiments our committee sent out samples of same and of a sample of fluidextract aconite to the physiological chemists of five different laboratories. The prime purpose of this was to determine whether results by such a minimum lethal dose method would be sufficiently close in the hands of varying laboratories and observers to warrant hoping to utilize it in an assay method—assuming, of course, that minimum lethal dose on guinea pigs would be a basis for therapeutic value. The results follow:

	Aconitine cryst. gm. per gm. wt. of guinea pig.	*F. E. Aconite Rt.*
Sharp & Dohme	.0000000625	0.000300
Upjohn	.0000000600	0.000266
Parke Davis & Co.	.0000000600	0.000300
Eli Lilly & Co.	.0000000625	0.000275
Norwich Pharmacal Co.,	.0000000510	0.000360

If we assume that minimum lethal dose on guinea pigs is a basis for therapeutic efficiency of aconite, then these results distinctly indicate that this method is sufficiently trustworhy and efficient to serve as an assay method to determine the therapeutic efficiency of aconite preparations based upon pure aconitine crystallized as a standard.

The Scientific Section of the American Drug Manufacturers' Association hence recommend that the chemical assay be dropped for aconite and its preparations and a physiological assay based upon aconitine crystallized U. S. P. be substituted in its place.

In my laboratory the m. l. d. for benzoyl-aconine and aconine were also determined on guinea pigs in comparison with the aconitine and the following results obtained:

	M. L. D. Guinea Pig.	
Aconitine cryst.	0.0000000625	gm. per gm. wt. of guinea pig.
Benzoyl-aconine	0.00002	gm. per gm. wt. of guinea pig.
Aconine	0.00025	gm. per gm. wt. of guinea pig.
F. E. Aconite Root ..	0.00003	gm. per gm. wt. of guinea pig.

These results indicate that aconitine is about 300 times as efficient, *i. e.*, toxic as benzoyl-aconine, and 4000 times as toxic as aconine, and at the same time they apparently possess practically none of the characteristic properties therapeutically of the aconitine—as for instance, producing numbness on the tip of the tongue, etc.

The method employed in these experiments was for the Fluidextract Aconite to dilute 1 c. c. thereof to 10 c. c. with 50 per cent. alcohol. Use 300 to 400 gm. guinea pig and calculate the dose per pig and dilute this with normal salt solution to a total volume of 1.5 c. c. per pig. Inject this into the subcutaneous tissues of the abdomen and take as a lethal dose the smallest amount which will kill within 24 hours.

For the Aconitine—disolve 0.1 gm. in 100 c. c. of 2 per cent. acetic acid. Dilute 1 c. c. of this solution to 10 c. c. with distilled water, givin a 1 : 10000 solution of aconitine. Calculate the total dose required for a pig of 300 to 400 gm. and dilute with normal saline solution to a sum total of 1.5 c. c. and inject as for the Fluidextract Aconite. Approximately 0.00000005 per gram is usually the lethal dose.

With the aconitine cryst. above used as a standard it will now remain to establish by comparative tests in various laboratories the extent of agreement reached in the application of above method of physiological assay for fluidextract and tincture aconite as well as the drug aconite, which latter will of course only be an application of the method of the two fluid preparations, as a liquid extract will have to be prepared to make the assay. This work is now before our Committee on Aconite and will doubtless be worked out some time soon.

PODOPHYLLUM ASH STANDARDS.

By E. L. Newcomb, C. H. Rogers and C. W. Folkstad,
MINNEAPOLIS, MINN.

The present criticism of the 3 per cent. ash limit for Podophyllum appears to be well-founded. Much of the drug on the market at the present time has been carelessly cleaned and should no doubt be rejected or properly cleaned before being used. On the other hand, some very well cleaned samples yield considerably more than the permitted 3 per cent. ash.

The results of our studies show that there is considerable variation in the proportionate amount of roots and rhizomes, that these parts are sometimes plump and sometimes shriveled. Plump starchy roots and rhizomes contain a proportionately small amount of calcium oxalate and yield a low ash. Shriveled roots and rhizomes contain less starch, proportionately more calcium oxalate and yield a high normal ash. Some commercial lots of the drug consist almost entirely of plump or bold roots and rhizomes. Others represent a mixture, while still other lots consist chiefly of shriveled roots and rhizomes.

An excess of inorganic foreign matter has no doubt been responsible for much of the difficulty with the ash standard. The factors above mentioned, however, play an important part not only in the ash yield, but also in the resin yield. In addition many samples contain an excess of organic foreign matter. There is real need for a purity rubric to provide for more uniform drug. The following results should be helpful in determining the standards to be adopted. The ash tests have been run by Mr. C. W. Folkstad, under the direction of Prof. C. H. Rogers.

ASH AND PURITY OF SAMPLES OF PODOPHYLLUM.

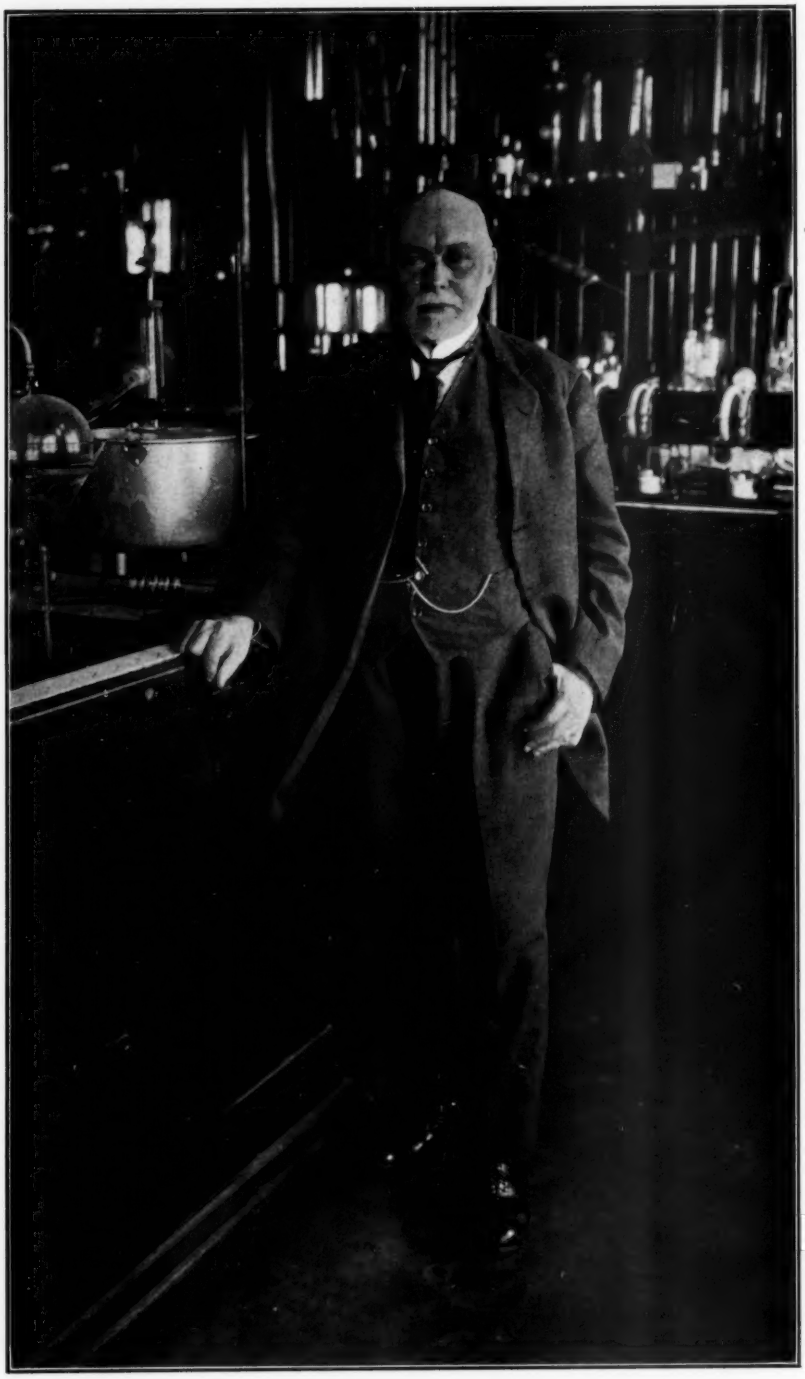
Sample No.	*Description.*	*% Total Ash.*	*% HCl. Insol. Ash.*
No. 1.	Prepared from carefully garbled commercial drug, bought 1920, powd. this Laby. 1920	2.51	0.34
		2.64	0.21
No. 2.	Commercial sample powdered, bought prior to 1916	3.35	0.30
		3.19	0.34
No. 3.	Commercial sample powdered, bought about 1916	4.08	1.07
		4.08	1.10
No. 4.	Commercial sample coarse powdered, from stock	3.34	0.51
		3.32	
No. 5.	Commercial powder, bought 1911, in carton labeled "No. 40 powder"	4.60	1.32
		4.55	1.23
No. 6.	Commercial powder, bought 1921, in carton, labeled "ash 4.40 per cent."	4.88	0.90
		4.86	0.86

Sample No.	*Description.*	*% Total Ash.*	*% H.Cl. Insol. Ash.*
No. 7.	Commercial powder, bought 1921, in paper bag, labeled "Podophyllum U. S. P. Mandrake Powdered, Analyzed and Guaranteed".....	8.88	5.95
		8.23	4.96
No. 8.	Sample prepared from 2-pound lot of whole podophyllum, bought in 1921, average portion powdered in this laboratory, 3-16-21. Not garbled ...	5.27	1.36
		4.74	0.96
No. 9.	Sample prepared from average portion of 2-pound lot of drug bought 1921, powdered in this laboratory, 3-16-21. Not garbled	2.47	0.24
		2.40	0.21
No. 10.	Sample prepared from 2-pound lot, bought 1921, average portion powdered in this laboratory, 3-16-21. Not garbled	3.73	0.66
		3.66	0.55
No. 11.	Sample prepared from rhizomes only, mostly shriveled, very little soil, rhizomes separated from drug bought 1921, powdered in this Laby. Rhizomes represented 86.9 per cent. of the drug. Garblings 0.8 per cent. ...	4.67	0.89
		4.35	0.64
No. 12.	Sample prepared from roots only, mostly shriveled, very little soil, drug same as No. 11, bought 1921, roots represented 12.2 per cent. of total weight, powdered in this laboratory, 3-24-21	7.28	0.37
		7.01	0.38
No. 13.	Sample prepared from rhizomes only, mostly plump, clean looking, drug bought 1921, rhizomes represented 89.1 per cent. of total weight, garblings 1.97 per cent. Rhizomes powdered in this laboratory, 3-24-21 ..	2.58	0.25
		2.77	0.25

Sample No.	*Description.*	*% Total Ash.*	*% HCl. Insol. Ash.*
No. 14.	Sample prepared from plump rhizomes only, clean looking, drug bought 1921. Rhizomes hand brushed and powdered in this Laby. 3-24-21	1.69	0.21
		1.63	0.18
No. 15.	Sample prepared from roots only, plump, clean looking drug bought 1921. Powdered in this Laby. Roots represented 9.11 per cent. of the total weight	3.69	0.87
		3.96	
No. 16.	Sample prepared from rhizomes only, some shriveled, some plump, drug bought 1921. Rhizomes represented 75.91 per cent. of total weight, garblings 6.97 per cent., rhizomes fairly clean looking, powdered in this Laby.,	3.93	0.96
		3.91	0.93
No. 17.	Sample prepared from shriveled rhizomes only same lot of drug as No. 16, powdered in this Laby.	5.09	0.66
		5.10	0.99
No. 18.	Sample prepared from roots only, some shriveled, same lot of drug as No. 16. Roots represented 16.4 per cent. of total weight, powdered in this Laby.	4.83	1.71
		4.81	1.83

Department of Pharmacognosy,
University of Minnesota.

GOLD MEDAL PRESENTED TO DR. FREDERICK B. POWER, PH. D., LL. D.



DR. FREDERICK B. POWER.

PRESENTATION OF MEDAL TO DR. FREDERICK B. POWER.

On Monday, May 9, 1921, in the Auditorium of the Cosmos Club, Washington, D. C., a very interesting event occurred when Mr. Henry S. Wellcome presented to Dr. Frederick B. Power a gold medal in recognition of his services as Director of the Wellcome Research Laboratories for a period of nearly twenty years prior to 1914.

Dr. David Fairchild opened the meeting by reading letters from the following gentlemen, expressing regret for their inability to attend the presentation: Dr. Thomas B. Osborne, of New Haven, Conn.; Prof. Marston T. Bogert, of Columbia University, New York City; Prof. Charles Baskerville, of the College of the City of New York; Prof. W. A. Noyes, of the University of Illinois, and Prof. Rodney H. True, of the University of Pennsylvania. After reading the letters he stated that the meeting was open.

Dr. Charles D. Walcott, Secretary of the Smithsonian Institution, and President of the National Academy of Sciences, then read the following presentation address:

"Ladies and Gentlemen—We have gathered here this afternoon to do honor to Dr. Frederick Belding Power, who for fifty years has spent his thinking hours among the complicated molecules of organic compounds; who, because he possesses that peculiar faculty of exhausting each subject which he takes up, has had the greatest influence both in America and Great Britain in raising the standard of our pharmacopœias; who has gained distinction by his most difficult and life-consuming researches into the chemical composition of plant compounds.

"As a lasting tribute to these fifty years of research and in commemoration of those which he spent as director of the Wellcome Chemical Research Laboratories of London, I have been asked by Mr. Henry S. Wellcome, their founder, to present him with this gold medal, which bears the following inscription:

"To

FREDERICK B. POWER, PH. D., LL. D.

In recognition of his distinguished services to science during 18½ years as Director of the Wellcome Chemical Research Laboratories, London.

Presented by the Founder,

HENRY S. WELLCOME, 1914.

"Doctor Power graduated from the Philadelphia College of Pharmacy in 1874, in the same class with his life-long friend, Mr. Wellcome, who urged him to pursue his studies in Germany. He spent the years from 1876 to 1880 in Strassburg, becoming the assistant to Dr. Flückiger, one of the greatest pharmacologists of Europe. Returning to America, he spent nine years in the organizing and building up of the Department and School of Pharmacy in the University of Wisconsin, four years in researches on essential oils in a newly organized chemical works near New York, and in 1896 Mr. Wellcome appointed him Director of his chemical research laboratories in London. For eighteen and one-half years he devoted his time exclusively to chemical research and the direction of a staff of research workers under him. One hundred and fifty important scientific memoirs were published from the laboratories during this period. These covered a wide field of investigation for which material was obtained from all parts of the world. Among these a very notable and complete study was made of the East Indian chaulmoogra oil, which resulted in the discovery of some physiologically active acids of an entirely new type. These form the basis of the new treatment of leprosy, which gives promise of effecting a complete cure of one of the most terrible diseases of mankind.

"During these years in London Dr. Power had the opportunity of meeting and forming the close friendship of the foremost scientific men of Great Britain. The recognition of his work by the leading chemists and other scientists of Europe would be perhaps exemplified in the high tribute paid to him by the late Lord Moulton, one of the most learned and versatile men in Europe who was entrusted by Kitchener with the task of producing the high explosives for the war. Shortly before his death, he chided Mr. Wellcome for permitting Dr. Power (who for family reasons had returned to America) to leave Great Britain, for, as he remarked, 'there was no one in Europe who could fill his place.'

"In 1908 the University of Wisconsin, commemorating the twenty-fifth anniversary of the formation of its Department of Pharmacy, conferred upon Dr. Power, its founder, the degree of LL. D., and in 1913 the Chemical, Linnean and Pharmaceutical Societies of London awarded him the Hanbury gold medal, a distinction only once perviously bestowed upon an American. This was followed by the presentation of an illuminated address and an album containing the signatures of contributors from many parts of the world.

"Dr. Power, in recognition of your distinguished services to science, and in commemoration of the years which you spent as director of a laboratory devoted to chemical research, I have the honor to present to you this gold medal of appreciation from your life-long friend, Mr. Henry S. Wellcome, who, although with us this afternoon, is unfortunately prevented by a severe throat affection from

addressing us himself. He wishes to explain in presenting it that war conditions have prevented its earlier execution and presentation."

Dr. Power acknowledged the medal as follows:

"Dr. Walcott, I feel it to be a great honor to receive at your hands the beautiful medal which my friend, Mr. Wellcome, has so kindly and generously bestowed upon me, and I deeply appreciate the sentiments you have so eloquently expressed concerning my work. I can assure you Dr. Walcott and Mr. Wellcome, that this memento will always be regarded by me as one of my most precious possessions. It is difficult and well-nigh impossible on an occasion such as this to adequately express in spoken words the thoughts that are uppermost in my mind, for there are many happy recollections when a friendship formed in boyhood has continued uninterruptedly during a period nearly half a century. I cannot but be reminded that it is just twenty-five years ago this month when I left America for London to undertake the organization of the Chemical Research Laboratories which Mr. Wellcome desired to establish, and that the first public announcement of his purpose was made on the evening of July 21, 1896, in a beautiful salon of the great metropolis, where, by the invitation of Mr. Wellcome, a number of the most distinguished scientific men of England were assembled, whom it was my privilege to meet. One of the guests on that occasion was the late lamented Lord Moulton, whose brilliant legal career and service to science, especially during the strenuous years of the war, have won for him an enduring fame. The work that was so auspiciously inaugurated on that July evening it was my privilege to conduct for a period of eighteen and one-half years, and, although years of hard and earnest toil, they were replete with many happy associations, and I trust not without some benefit to the science that it was my endeavor to serve.

"There is one dominating thought that I should like particularly to convey to my friend, Mr. Wellcome, and that is embodied in an expression of gratitude. I am grateful for the encouragement and inspiration received from him on our journey through life, for we have traveled long and far together, but above and beyond all I am grateful for having possessed through so many years so kind, generous and true a friend. For this latest expression of your kindness, Mr. Wellcome, I beg you to accept my warmest thanks, and I desire also to extend my hearty thanks to Dr. Walcott for having so happily conveyed to me your beautiful gift."

Dr. Walcott then adjounrned the formal meeting after inviting all those present to meet Dr. Power and to add a word of personal

appreciation to those given formally. A social hour followed, with light refreshments.

There was a distinguished gathering of notable persons present. Among the guests were:

Dr. Alexander Graham Bell; Hon. Robert Lansing; Dr. F. W. Clarke and Dr. David White, of the Geological Survey; Dr. Harvey W. Wiley; Dr. Carl L. Alsberg, Chief of the Bureau of Chemistry; Dr. W. A. Taylor, Chief of the Bureau of Plant Industry; Dr. L. O. Howard, Chief of the Bureau of Entomology; Dr. F. W. Coville, Dr. W. E. Safford, Prof. L. C. Corbett and Dr. O. Schreiner, of the Bureau of Plant Industry; Dr. Charles L. Parsons, Secretary of the American Chemical Society; Dr. W. F. Hillebrand, U. S. Bureau of Standards; Dr. Marcus Benjamin and Dr. J. N. Rose, of the Smithsonian Institution; Prof. Charles E. Munroe, National Research Council; Admiral Brownson, General R. E. Noble, of the Surgeon General's Office of the U. S. Army; Rear Admiral William C. Braisted, President of the Philadelphia College of Pharmacy and Science; Mr. Howard B. French, former President of the Philadelphia College of Pharmacy and Science; Hon. John B. Payne, former Secretary of the Interior; Rev. Charles Wood, Church of the Covenant; Senator Richardson; Dr. Atherton Seidell, of the Hygienic Laboratory; Mrs. (General) Gorgas; Professors Charles H. LaWall, E. Fullerton Cook and Julius W. Sturmer, and former President Otto W. Osterlund, of the Philadelphia College of Pharmacy and Science; Dr. Lyman F. Kebler, V. K. Chestnut, E. K. Nelson, and many others from the Bureau of Chemistry.

THE MULFORD BIOLOGICAL EXPLORATION.

The early plans for the scientific expedition, known as the Mulford Biological Exploration of the Amazon Basin, were made public in an article appearing in the AMERICAN JOURNAL OF PHARMACY, issue of November, 1920.

The many groups of scientists and laymen who have shown such great interest in the plans for this work will be interested to know that the work is now under way, and that the expedition made its departure from New York on June 1st, under the most favorable circumstances.

The delay in getting the expedition into the field has been caused

by a chain of circumstances which have necessitated considerable changes in the original plan and in the route to be followed. One of the causes for the delay, which has given a great deal of concern to those interested, was the illness of the Director, Dr. H. H. Rusby, Dean of the College of Pharmacy of Columbia University. Dr. Rusby has been suffering from a severe and prolonged attack of pleuro-pneumonia, which struck him down very suddenly in the midst of active preparations for his trip. His many friends in the medical and pharmaceutical professions and among botanists will be pleased to learn that he is now well on the road to complete recovery.

The enforced delay has not been without benefit. From one point of view it has been of actual advantage, in that ample time was afforded for the elaboration of plans and preparations in the greatest possible detail. It has also resulted in the enlargement of the scope of the work to be undertaken and in the personnel of the party.

Membership in the party as now constituted, includes Dr. H. H. Rusby, as Director, who will be accompanied by a secretary, personal assistant and taxidermist in the person of George S. McCarty, a young man of sportsman-like qualities and training, from a well-known family of Woodbury, N. J.

Dr. Rusby will also be accompanied by Dr. Wm. M. Mann, an Entomologist of the Bureau of Entomology, U. S. Department of Agriculture, and Honorary Custodian in the Division of Insects, U. S. National Museum. Dr. Mann is an explorer and collector of wide experience in tropical travel.

E. N. Pearson joins the party as Ichthyologist, representing Dr. C. H. Eigenmann, of the University of Indiana, and Dr. A. G. Ruthven, of the University of Minnesota.

The botanical work of the expedition will be greatly increased by the addition to the party of Dr. Orland E. White, of the Brooklyn Botanic Garden, who goes as representative of the Brooklyn Botanic Garden and of the Bussey Institution of Harvard University.

He will devote his energies to the collection of orchids for Dr. Ames, and to the study of the economic botany of the regions covered.

The complete study of the medicinal products will occupy the attention of many specialists. Dr. Rusby will himself undertake

their botanical classification and description. Their microscopical study will be pursued by Dr. Ballard at the Columbia University School of Pharmacy by Professor Youngken, Philadelphia College of Pharmacy and Science, Schneider of Nebraska, Newcomb of Minnesota, and others. Their chemistry will be studied by Arny of Columbia, Jordan of Purdue, Sayre and Havenhill of Kansas. The study of their physiological and medicinal properties will occupy the attention of many medical men at Yale, Harvard, the University of Pennsylvania, Johns Hopkins, and connected with the American Medical Association headquarters at Chicago.

Among other subjects of interest, is that of oil-seeds, of which there is a vast variety in the forests of tropical America. From fifty to a hundred pounds or more of each of these will be collected as encountered and these will be shipped home for expression and the study of their oils. Professor Augustus A. Gill, of the Boston Institute of Technology has undertaken to pursue these researches. Similarly there are very many plants containing essential oils that are likely to prove of value, and Dr. Edward Kremers, of the University of Wisconsin will interest himself in the study of these. The region to be traversed abounds in serpents and other reptiles, both poisonous and innocent. These will be preserved like the fishes. The batrachians will be sent to Professor Ruthven, of the University of Michigan, and the others to the American Museum of Natural History in New York City.

Special interest attaches to the arrangements recently completed, by which Dr. F. L. Hoffman, Vice-President and Chief Statistician of the Prudential Life Insurance Company, will accompany Dr. Rusby and his party for at least part of the journey. Dr. Hoffman, as one of the Directors of the American Public Health Association, and one of the leaders in the public health movement, has been interested in the plans for this expedition from the beginning. He joins the expedition with a very broad object in view, being especially interested in the health, longevity and sanitary progress in the regions visited, particularly as regards American residents, temporarily or permanently settled under conditions of tropical life. Knowing the rich natural resources of these regions he shares with Dr Rusby a vision of the possibilities of wonderful development along many lines—a development which is now greatly retarded chiefly on account of an unfavorable environvent and a high mortality, due

largely to diseases caused by insects and parasites of various kinds, which sap the vitality of the people.

Dr. Hoffman's efforts will be directed toward the accumulation and correlation of as much information as possible on these subjects. In fact it is planned to stress the economic phases of the entire work of the expedition with the aim of adding much to the knowledge necessary before any practical means can be employed to lessen mortality; to improve the environment and to make life more comfortable and worth living under tropical conditions.

From the library of the Prudential Insurance Company at Newark, the expedition has been supplied with copies of the latest maps of the regions to be visited, and copies of important publications and records of previous expeditions and notes on the tropical diseases occurring there—all of which will contribute greatly to the success of the work.

The change in the date of departure has made necessary a complete reversal of itinerary, in order to take advantage of the dry season north and south of the equator. Dr. Rusby and party will proceed directly to La Paz, Bolivia, from which city they will set out about July 1st, their first objective being the town of Rurenabaque, on the eastern side of the Andes. Here temporary headquarters will be established while the surrounding regions are being explored. Some of the party will proceed thither via the La Paz River, making collections en route in previously untouched territory. Others of the party, with the main portion of the cargo, will go by way of the Guggenheim Mines of the Bopi River. The first part of this journey is over a fine automobile road built by the Guggenheim Brothers to their large mines near Asunto. Both Mr. Daniel and Mr. Murray Guggenheim are active and generous officers and managers of the New York Botanical Gardens, and are largely interested in this expedition. They have promised every assistance that their representatives in Bolivia can render.

The next objective will be Lake Rocagua, in which region they expect to spend a month or more exploring and collecting. Other important collections will be made in the Valleys of the Rio Beni and the Mamore. The Mamore River will be visited with the special object of exploring the region which yields Brazilian Ipecac. Temporary headquarters will next be established at Villa Bella, the western terminus of the Madeira-Mamore Railroad. The party will so

arrange their work and time their journey as to reach Manaos about November of this year. Here they will recive large shipments of supplies for the second half of the journey and send home the collections already made.

According to present plans the party will then start out from Manaos early in 1922, ascending the Rio Negro and Rio Uaupes for the purpose of exploring and collecting among the upper waters of the latter river and in some of the valleys and ravines along the eastern side of the Andes, south of Bogota, Colombia. After crossing the mountains to Bogota, they will finally emerge at the coast at Barranquilla for their return journey.

To many experienced tropical travelers the plans for the second half of this journey from Manaos to Bogota appear to be somewhat venturesome and impractical because the party may be expected to be very much exhausted upon their arrival at Manaos. Dr. Rusby is confident, however, they will all arrive at Manaos in good health and, after a short rest, will be in good condition to undertake the second half of their journey.

Perhaps no other expedition that has gone into South America has ever entered the tropics so well protected medically against possibilities of fevers, skin diseases and the numerous tropical affections. The medical supplies which the expedition is taking includes a very long list of standard pharmaceuticals and a number of biological products, which are of even greater importance under the circumstances. These include great quantities of antidysenteric serum, for the prompt treatment of cases of dysentery, should any of the members of the party contract that disease,—a rather unlikely event if all the members make the proper use of the means provided for the sterilization of the drinking water. Antipneumococcic Serum and antitetanus serum are also included among the supplies. Most important, however, is a quantity of anti-snake-venom, which the Mulford Company took special pains to prepare for Dr. Rusby's party and which they are supplying to them in small, sterile, hypodermic syringes, ready for instant use when occasion requires.

Members of the party have further protected themselves against disease by taking certain preventive measures. These include the well-known measures of vaccination against smallpox and the prophylactic inoculations against Typhoid Fever, the effectiveness of which no longer remains a matter of doubt. In view of the

prevalence and dangers of pneumonia, to which they are exposed, especially in the highlands of Bolivia, the members of the party have been provided with an antipneumonia vaccine, which should give them considerable protection, for some time at least. If it gives them a moderate protection against pneumonia for even six or eight weeks, this will carry them over the most dangerous period, *i. e.*, until they have crossed the Andes and have descended from the highlands of Bolivia to the great plains. They are also supplied with various insecticides and repellents which they will use to obtain relief from the annoyance of incessant attacks of hordes of insects.

Through Dr. Rusby's wide experience and foresight, all the possible needs of the party while in the field have been provided for in great detail. Among the supplies are large quantities of foodstuffs, such as canned meats, bacon, etc., purchased from surplus Army stores, and also a quantity of evaporated vegetables and soup powders. Their supplies and equipment, weighing nearly three tons, is packed in a large number of boxes of the proper size for transportation by mule or human porters.

The scientific work of the expedition is well provided for in the form of all kinds of scientific apparatus, collecting equipment and containers with abundant supplies of formaldehyde and other preservatives. A full supply of printed labels and note-books are among the details provided, so that collections may be sent back properly identified and ready for study.

The active support and co-operation which has come to Dr. Rusby from so many quarters is a source of much gratification, and the many offers of assistance and tokens of interest and esteem have greatly encouraged the members of the party as they start out on this most difficult undertaking.

The officials of the H. K. Mulford Company, which house is acting as sponsor and financial backer of this enterprise, have been especially gratified at the generous attitude which institutions of learning and Government Bureaus have taken toward this expedition.

The hope has been expressed in many quarters that the successful outcome of this enterprise will convince scientists and the public generally that complete and hearty co-operation betwen large industrial and scientific institutions can be obtained to their mutual benefit and on a thoroughly professional and altruistic basis.

ABSTRACTED AND REPRINTED ARTICLES

A COLOR REACTION FOR ACONITE.*

By S. MALLANNEH, M. D., D. P. H.

The color reactions at present known are not reactions of aconitine, but of benzoic acid, which is one of the products of decomposition of aconitine. Hence the color reactions are not specific.

Most of the color reactions for alkaloids are such that they are useful only when applied to pure samples of alkaloids, but they are of no use when applied to crude substances containing alkaloids.

In medico-legal cases, especially in India, the poisoning is generally caused by the administration of crude substances in the form of powdered root, bark, or seeds, and not by the use of active principles. If the quantity of the vegetable poison present in the stomach be small, as is generally the case with aconite, it is next to impossible in most cases to get a sufficient amount of alkaloid extracted in order to prove the presence of poison by means of experiments on animals.

In India the vegetable poison also undergoes decomposition so quickly that it is almost impossible to detect its presence in a dead body, though distinct clinical symptoms of poisoning might have been present before death. But the cause of the failure to detect the poison in such cases is that, up to date, there is no reliable chemical test known for aconite.

As the result of my experiments, I have discovered a test which I think is very useful for medico-legal purposes. If a minute particle of potassium ferricyanide be placed close to a minute portion of aconitine or a small portion of powdered root of aconite, and then a drop of formic acid added, a green coloration immediately appears. This is every delicate reaction as 1/8000 grain of aconitine gives a positive reaction. Heat should not be applied for this test.

Morphine, atropine, digitalin, strychnine, eserine and hyoscya-

* Reprinted from *The Analyst*, May, 1921.

mine do not react to this test, which therefore seems to be specific for aconite. It is not only applicable to the pure alkaloid, but also applicable to powdered root of aconite. Hence, if confirmed, it will be of great toxicological importance. Recently, in a case of human poisoning at Banswada Nizamaabad, I was able to test this reaction. A few black fragments found adherent to the stomach wall of the deceased gave positive reaction to this test, and the case was confirmed subsequently by experiments on animals. The police were able to procure from the house of the culprit a brown powder, which on examination was found to be powdered root of aconite.

DISCUSSION.

Mr. H. Finnemore said that, apart from the limited value of all color reactions, this test was not specific for aconitine, since it appeared to be given by the Indian variety of aconite, which contained pseudoaconitine, but not aconitine.

WOOD DISTILLATION.

Census Bureau's Summary Concerning the Industry, 1919.

A preliminary statement of the general results of the 1919 census of manufactures with reference to the wood distillation industry has been issued by William M. Steuart, Director, Bureau of the Census, Department of Commerce. It consists of a detailed statement of the quantities and values of the various products manufactured, prepared under the direction of Mr. Eugene F. Hartley, Chief Statistician for Manufactures.

Reports were received from 116 establishments engaged in the distillation of wood, and their products for the year were valued at $32,635,000. At the census of 1914 there were 101 establishments, with products valued at $10,530,000. The value of annual production has therefore increased $22,105,000, or 209.9 per cent.

In 1919, 44 establishments were located in Pennsylvania, 21 in New York, 16 in Michigan, 7 in Georgia, 6 in Florida, 4 in Alabama, 4 in Louisiana, 3 in Wisconsin, 2 in Mississippi, 2 in North Carolina, and 1 each in Connecticut, Kentucky, Missouri, New Jersey, Tennessee, Texas and West Virginia.

The statistics for 1919 and 1914 are summarized in the follow-

ing statement. These figures are preliminary and subject to such change and correction as may be necessary from a further examination of the original reports.

Comparative Summary of Statistics for the Wood Distillation Industry, 1919 and 1914.

		1919.	1914.
Number of establishments[1]		116	101
Value of products[1]		$32,635,000	$10,530,000
Wood alcohol (for sale):			
Crude	Gals.	6,981,000	7,197,000
	Value	$5,593,500	$1,605,900
Refined	Gals.	6,985,000	6,235,000
	Value	$8,381,900	$2,709,400
Acetate of lime	Lbs.	152,064,000	163,522,000
	Value	$2,682,200	$2,138,900
Turpentine, wood	Gals.	1,521,000	575,600
	Value	$1,207,700	$194,200
Rosin, wood	Bbls. (280 Lbs.)	[2]234,000	51,800
	Value	$2,742,600	$198,200
Charcoal	Bush.	48,499,000	44,828,000
	Value	$8,231,400	$2,829,600
Other wood products and derivatives		[3]$3,243,000	$626,300
All other products		$552,700	$227,500
Materials.			
Wood	Cost	$8,323,000	.....
Hard woods	Cords	1,019,500	970,300
Pine	Cords	255,700	72,200
Crude wood alcohol purchased	Gals.	7,360,000	5,665,000
	Cost	$5,898,000	$1,408,000

[1] Includes one establishment in 1919, and six in 1914, engaged primarily in other industries; subsidiary products in 1914, $647,292.

[2] Includes 12,254 bbls. reclaimed from gum rosin dross.

[3] Includes for 1919: Tar oil, 803,440 gals., $240,805; tar, 2,143,157 gals., $481,820; wood creosote, 1,152,655 lbs., $31,957; methyl acetone, 930.253 lbs., $134,166; ketone, 269,984 lbs., $52,141, and formaldehyde, acetone and acetone oil, each the product of two establishments, and acetic acid and acetate of soda, each one establishment.

SCIENTIFIC AND TECHNICAL ABSTRACTS

TOXICITY OF THYMOL AND CARVACROL.—Dr. A. E. Livingston, of the Hygienic Laboratory, has recently published the results of an extensive investigation of the comparative toxicity of thymol and carvacrol. He reports: the toxicity of thymol and carvacrol on rabbits is essentially the same; the toxicity of thymol and carvacrol as tested on paramecia shows no striking difference; tests on earthworms indicate that the relative anthelmintic values of thymol and carvacrol are practically the same. (*J. Pharm. Esp. Ther.*, Vol. 17, p, 261, 1921.)

J. F. C.

IDENTIFICATION OF TR. COLCHICUM.—Glücksmann suggests the following procedure for the identifying of this tincture: 1. A dull yellow solution results from the mixing of 1 ml. Tr. Colchicum and 9 ml. conc. hydrochloric acid. 2. Mayer's test. 3. 25 ml. of tincture to which is added 0.5 Gm. paraffin are evaporated with shaking on the steam bath shaken up with 6 ml. of distilled water, cooled, filtered, the residue washed and the filtrate evaporated to dryness, extracter with 10 ml. warm chloroform and filtered after adding a little asbestos. The chloroform is evaporated off, the residue is dissolved in about 5 ml. of water and filtered if necessary. The clear solution is treated with 1 to 2 drops of 10 per cent. ferric chloride solution and 10 drops of strong hydrochloric acid, and is maintained several minutes at the boiling point in order to convert the colchicine into colchicein. By this treatment the green color which develops becomes more intense. If this is not sufficiently decisive the cooled solution is shaken with an equal volume of chloroform, which, after several days, becomes colored cherry red. (*Apoth.-Ztg. der tschechoslowakischen Republic*, 1920, p. 328.)

J. F. C.

CUPRESSUS SEMPERVIRENS IN THE TREATMENT OF HEMORRHOIDS.—The cypress has vaso-constrictive properties analogous to hamamelis; these are even more marked and more constant than those of the latter. The fluidextract, tincture or soft extract may be given internally in doses which represent from 10 to 30 grains twice a day. For local application the tincture or fluidextract may be made into a lotion, the soft extract may be used in an ointment or in suppositories. Good results have followed this treatment. (Leclerc, *Bull. Soc. Thérap.*, 1920, p. 184.)

J. F. C.

COTTON'S PROCESS ETHER.—Some time ago, J. H. Cotton[1] claimed that there were present in anæsthetic ethers two classes of extraneous substances: one class including substances favorable to the production and maintenance of anæsthesia and which were really synergists, while the other class consisted of undesirable impurities, which cause post-operative nausea, irritation of the respiratory tract, and other symptoms generally recognized as "ether sickness." He said that by supercharging purified ether with the beneficial synergists—ethylene and carbon dioxide—he could produce a condition of analgesia, without loss of consciousness, with less ether than was necessary for surgical anæsthesia.

This new ether has been reported on by J. E. Lumbard,[2] who found that pure ether, 99.8 per cent., simply acted like a very weak ether, while ordinary 96 per cent. ether produced satisfactory anæsthesia on the same patients. The ideal ether, he thinks, would therefore be a superior grade of ether from which toxic properties had been eliminated, afterwards recharged with the synergists in suitable proportion, just as Cotton claims. Such an ether he has tried in over 400 cases, and he concludes that it certainly acts like a stronger ether, at least during the stage of induction, in which there is apparently less irritation of the mucous membranes and less secretion of mucus. During the stage of maintenance little difference was noted, unless possibly that a smaller amount of ether was used. Recovery seemed less disturbed than when using ordinary ethers, and post-anæsthetic effects were minimized. There is greater tendency

[1] *Amer. J. Surg.*, April, 1919, p. 34.
[2] *Ibid.*, October, 1920.

to cyanosis, and patients have to be more carefully watched. Analgesia by Cotton's ether is apparently identical with primary anæsthesia such as can be obtained with any other anæsthetic, but it is possible with the new ether to maintain the analgesic state for a much longer time, with the patient fully conscious and with fairly good control of all voluntary muscles. (From the *Prescriber,* No. 176, 194; May, 1921.)

Preparation of Pure Carbon Dioxide.—Robert Crosbie Farmer, of the Royal Arsenal, Woolwich, prepares carbon dioxide completely free from air by the reaction between potassium hydrogen carbonate and sulphuric acid. Carbon dioxide is passed through a solution of potassium hydrogen carbonate (300 grams to the litre) and also through a solution of sulphuric acid (120 cc. diluted to 1 litre); the solutions are thus rendered free from dissolved air; they are then caused to react in an air-free vessel; and pure carbon dioxide, entirely free from air, is obtained. The product is so pure that it gives practically no gaseous residue on absorption with potassium hydroxide solution. (*Journal of the Chemical Society,* 1920, cxvii, 1446-1447; through *Journ. of the Franklin Inst.,* Feb., 1921.)

A Qualitative Reaction for Magnesium.—F. Eisenlohr describes the following test for magnesium. An alcoholic solution of alkanet root is prepared and to 5 cc. of it is added a drop of ammonium carbonate solution of 2N strength. This produces no appreciable change of color, but if additions are made of a few drops of neutral solutions of either magnesium, barium, calcium, strontium or manganous salts the following effects are respectively produced:

Magnesium	Barium	Calcium	Strontium	Manganese (ous)
blue violet	no change	blue	blue violet	blue violet

The colorations produced by magnesium, strontium and manganous salts are not strikingly different, but if the solution is acidified with not more than two drops of 2N hydrochloric acid, the liquid changes to bright red, and then, if again rendered alkaline by a like volume of ammonium carbonate solution, becomes, in the presence of magnesium, blue violet. In dealing with an ordinary phosphate precipitate, this is dissolved in 2N hydrochloric acid, and a

portion of the alkanet solution is mixed with a drop of the acid solution, and then one to two drops of the ammonium carbonate solution, when the presence of a magnesium compound will be shown by the production of the blue violet. If magnesium is not present, the original color of the alkanet solution will appear.

The alkanet solution must not be diluted with water, as this will give rise to a hydrolysis of the ammonium carbonate by which ammonium hydroxide will be produced (*Ber.*, 1920, Vol. liii, 176; through *Journ. Franklin Inst.*, Feb., 1921.)

MEDICAL AND PHARMACEUTICAL NOTES

ANTIBODY STUDIES.—*The Journal of Immunology*, for March, 1921, was devoted exclusively to the publication of "Antibody Studies," by Dr. F. M. Huntoon, of the Mulford Biological Laboratories, Glenolden, Pa.

These papers cover a vast amount of original research work, on a very important subject, and have to do with extracting the protective substances or antibodies from bacterial serums, such as Antipneumococcic Serum, Antimeningococcic Serum, etc.

The results of Dr. Huntoon's work hold promise of a new epoch in the serum treatment of pneumonia, and possibly some of the other infectious diseases. Dr. Huntoon was able to produce sterile extracts of the pneumococcic protective antibody, possessing approximately the same antibody content as the best immune serum, and yet very low in serum protein content.

We are informed that these extracts have not yet been placed on the market, but their clinical value is being carefully determined in a number of leading hospitals, and we are assured that if the results continue satisfactory, these antibody extracts will be made available by the Mulford Laboratories as soon as possible, for the benefit of the medical profession, and humanity at large.

LOBINOL—THE POISON OF POISON OAK.—James B. McNair has extracted a dermatitant, or poison, producing inflammation of the skin, from the poison oak *Rhus diversiloba*. The bark was extracted

with alcohol; and the extracted poison was purified by successive treatments with petroleum, ether, alcohol, sodium chloride brine, and distilled water. The poison apparently is an unsaturated compound of the aromatic series, containing carbon, hydrogen, and oxygen; it reacts like a phenol, and may contain two hydroxyl groups in the ortho position. On account of its phenolic nature, it has been named lobinol. (*Journ, Amer. Chem. Soc.,* 1921, xliii, 159-164; through *Journ. Frank. Inst.,* Feb., 1921.)

NEWS ITEMS AND PERSONAL NOTES

FUNDS FOR SCIENTIFIC RESEARCH.—The Research Information Service of the National Research Council has recently compiled information about funds for scientific research. From this compilation it appears that there are hundreds of special funds, trusts, or foundations for the encouragement or support of a research, in the mathematical, physical and biological sciences, and their applications in engineering, medicine, agriculture and other useful arts. The income from these funds, which amounts annually to at least fifty million dollars, is used principally for prizes, medals, research scholarships and fellowships, grants and sustains appropriations or endowments.

So numerous have been the requests to the Research Council for information about sources of research funds, availability of support for specific projects and mode of administration of particular trusts or foundations, that the Research Information Service has created a special file, which it is proposed to keep up to date in order to answer the questions of those interested in such funds. Furthermore, in order to give wider publicity to the immediately available information about research funds, the Council has issued a bulletin under the title *"Funds Available in 1920 in the United States of America for the Encouragement of Scientific Research."*

Inquiries concerning the bulletin or for information about research funds should be addressed, National Research Council, Information Service, 1701 Massachusetts Avenue, Washington, D. C.

INFORMATION BUREAU OF THE NATIONAL RESEARCH COUNCIL. —Many scientists lack the library facilities which their work demands. They are compelled either to journey to distant libraries or to try to borrow books by mail. Often it is difficult for them to locate some thing that is badly needed, and again it may be impossible to borrow it.

The Research Information Service of the National Research Council is prepared to assist investigators by locating scientific publications which are not generally or readily accessible. It will also, as is desired, have manuscripts, printed matter or illustrations copied by photostat or typewriter. The cost of copying varies from ten to twenty-five cents per page. No charge is made for this service unless an advance estimate of cost has been submitted and approved by correspondent.

Requests for assistance should be addressed, National Research Council, Information Service, 1701 Massachusetts Avenue, Washington, D. C.